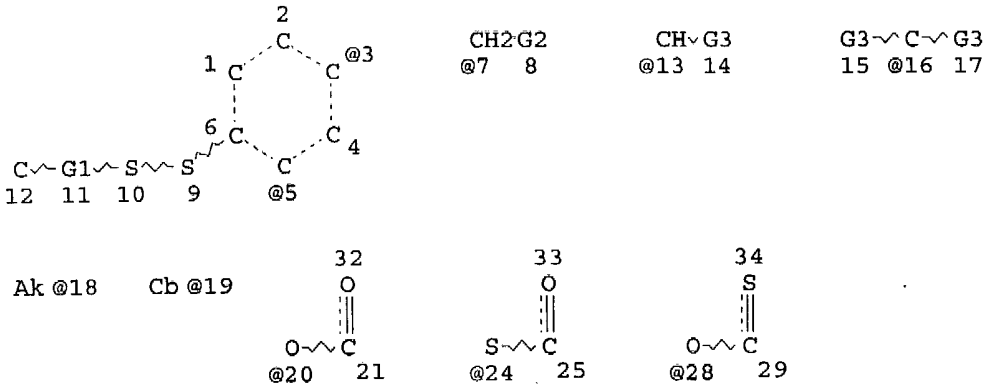
=> d que l14
L8 STR



VAR G1=CH2/13/16
VAR G2=20/24/28
VAR G3=18/19
VPA 7-3/5 U
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 18
CONNECT IS E1 RC AT 19
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 19
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M6 C AT 19

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L10 44 SEA FILE=REGISTRY SSS FUL L8
L11 44 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND N/ELS
L12 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L13 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND LIPOSOM?
L14 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 OR L13

=> d l14 ibib abs hitind hitstr 1-12

L14 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:861161 HCAPLUS
DOCUMENT NUMBER: 140:64928
TITLE: Fully Detachable Molecular Umbrellas as Peptide Delivery Agents
AUTHOR(S): Jing, Bingwen; Janout, Vaclav; Regen, Steven L.
CORPORATE SOURCE: Department of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA
SOURCE: Bioconjugate Chemistry (2003), 14(6), 1191-1196
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A persulfated mol. umbrella, derived from cholic acid and spermidine, has

been covalently attached to H-Tyr-D-Ala-Gly-Phe-D-Leu-OH (DADLE) by use of an o-dithiobenzyl carbamate linkage. Treatment of the resulting conjugate (I) with glutathione in solution resulted in the liberation of the free form of the peptide. Addition of I to glutathione-entrapped **liposomes**, prepared from 1-palmitoyl-2-oleyol-sn-glycero-3-phosphocholine (POPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylglycerol (POPG), and cholesterol [POPC/POPG/cholesterol, 72:4:24 (mol/mol/mol)], resulted in the delivery of DADLE into their aqueous interior.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 34

IT Membrane, biological
(bilayer, **liposome** model of, crossing of; preparation of fully detachable mol. umbrellas as peptide delivery agents)

IT 63631-40-3, DADLE
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efflux of, from cholesterol-rich **liposomes**; preparation of fully detachable mol. umbrellas as peptide delivery agents)

IT 70-18-8, Glutathione, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**liposome**-entrapped; preparation of fully detachable mol. umbrellas as peptide delivery agents)

IT 57-88-5, Cholesterol, biological studies 26853-31-6, 1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine 185435-28-3, 1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylglycerol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**liposomes** containing, crossing of; preparation of fully detachable mol. umbrellas as peptide delivery agents)

IT **639458-82-5P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of fully detachable mol. umbrellas as peptide delivery agents)

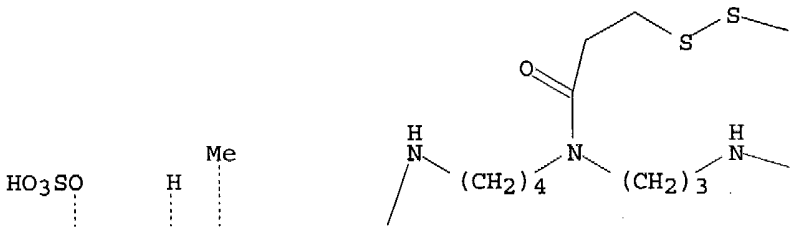
IT **639458-82-5P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of fully detachable mol. umbrellas as peptide delivery agents)

RN 639458-82-5 HCAPLUS

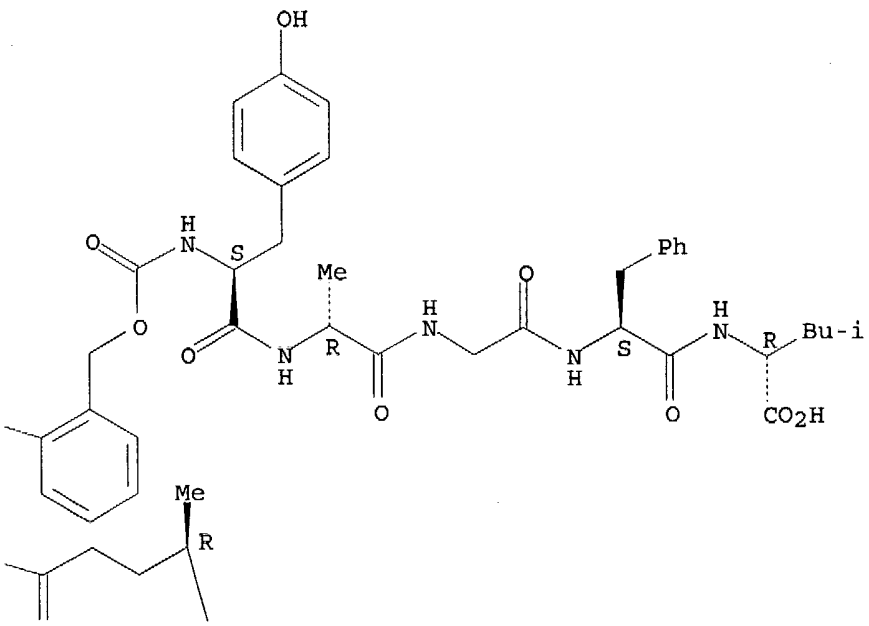
CN D-Leucine, N-[[[2-[[3-oxo-3-[[4-[[(3α,5β,7α,12α)-24-oxo-3,7,12-tris(sulfooxy)cholan-24-yl]amino]butyl][3-[[(3α,5β,7α,12α)-24-oxo-3,7,12-tris(sulfooxy)cholan-24-yl]amino]propyl]amino]propyl]dithio]phenyl]methoxy]carbonyl]-L-tyrosyl-D-alanylglycyl-L-phenylalanyl-, hexasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

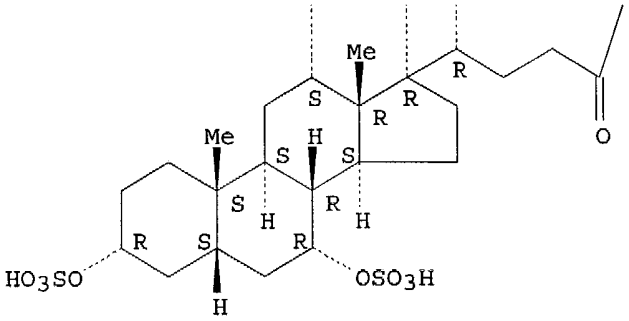
PAGE 1-A



PAGE 1-B

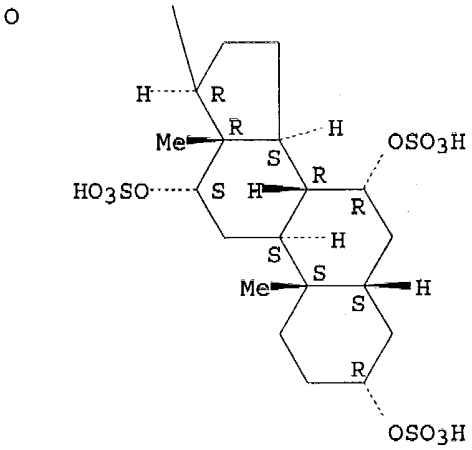


PAGE 2-A



●6 Na

PAGE 2-B



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:118404 HCAPLUS
DOCUMENT NUMBER: 138:158765
TITLE: **Liposome** composition for delivery of nucleic acid
INVENTOR(S): Huang, Shi-kun; Zalipsky, Samuel; Zhang, Wei-ming
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U. S. 6,342,244.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003031704	A1	20030213	US 2001-20671	20011212
US 6342244	B1	20020129	US 2000-556056	20000421
US 2002128195	A1	20020912	US 2001-982336	20011015
US 6605299	B2	20030812		
US 2003054028	A1	20030320	US 2002-57839	20020125
WO 2003053409	A1	20030703	WO 2002-US41461	20021205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003211079	A1	20031113	US 2003-371169	20030221

PRIORITY APPLN. INFO.:

US 1999-130897P	P	19990423
US 1999-158693P	P	19991008
US 2000-556056	A2	20000421
US 2000-685940	A2	20001010
US 2000-556610	A1	20000421
US 2001-982336	A1	20011015
US 2001-20671	A1	20011212

OTHER SOURCE(S): MARPAT 138:158765

AB A **liposome** composition for delivery of a nucleic acid in vivo or ex vivo is described. The **liposomes** in the composition are comprised of (i) a lipid that is neutral in charge at physiol. pH and pos. charged at pH values less than physiol. pH and (ii) a lipid joined to a hydrophilic polymer by a dithiobenzyl linkage. The **liposomes** are associated with a nucleic acid for delivery to a cell.

IC ICM A61K009-127
ICS A61K048-00

NCL 424450000; 514044000

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

ST gene delivery **liposome** compn

IT Selectins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E-; **liposome** composition for delivery of nucleic acid)

IT Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E-selectin; **liposome** composition for delivery of nucleic acid)

IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(L-, receptor; **liposome** composition for delivery of nucleic acid)

IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P-, receptor; **liposome** composition for delivery of nucleic acid)

IT Endocytosis
(by tumor cells; **liposome** composition for delivery of nucleic

acid)
IT Neoplasm
(endothelial; **liposome** composition for delivery of nucleic acid)
IT Blood vessel
(endothelium, tumor; **liposome** composition for delivery of nucleic acid)
IT Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(folate; **liposome** composition for delivery of nucleic acid)
IT Gene therapy
(**liposome** composition for delivery of nucleic acid)
IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**liposome** composition for delivery of nucleic acid)
IT CD4 (antigen)
Vascular endothelial growth factor receptors
neu (receptor)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**liposome** composition for delivery of nucleic acid)
IT DNA
Nucleic acids
Oligonucleotides
RNA
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**liposome** composition for delivery of nucleic acid)
IT Polyoxyalkylenes, biological studies
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**liposome** composition for delivery of nucleic acid)
IT Drug delivery systems
(**liposomes**; **liposome** composition for delivery of nucleic acid)
IT Encapsulation
(microencapsulation; **liposome** composition for delivery of nucleic acid)
IT CD19 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors; **liposome** composition for delivery of nucleic acid)
IT Drug delivery systems
(targeted; **liposome** composition for delivery of nucleic acid)
IT Fibroblast growth factor receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 1; **liposome** composition for delivery of nucleic acid)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αβ-, receptor; **liposome** composition for delivery of nucleic acid)
IT 62031-54-3, Fgf 62229-50-9, Egf
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**liposome** composition for delivery of nucleic acid)
IT **495399-53-6P**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**liposome** composition for delivery of nucleic acid)

IT 9003-09-2, Polyvinylmethylether 9003-11-6, Polyethyleneoxide-polypropyleneoxide copolymer 9003-39-8, Polyvinylpyrrolidone 9004-62-0, Hydroxyethylcellulose 9086-85-5, Polyhydroxypropylmethacrylate 25014-12-4, Polymethacrylamide 25322-68-3, Polyethyleneglycol 25805-17-8, Polyethyloxazoline 26022-14-0, Polyhydroxyethylacrylate 26375-28-0 26793-34-0, Polydimethylacrylamide 37353-59-6, Hydroxymethylcellulose 40704-75-4 158606-68-9, Polyaspartamide 158820-12-3
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**liposome** composition for delivery of nucleic acid)

IT 51-45-6, 1H-Imidazole-4-ethanamine, reactions 78-96-6, 1-Amino-2-propanol 100-28-7 104-03-0 106-89-8, reactions 616-30-8 7693-46-1 13552-21-1, 1-Amino-2-butanol 51023-28-0 51063-97-9 53339-53-0 103511-22-4 173584-30-0 210297-55-5 495399-48-9 495399-49-0 495399-50-3 495399-52-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(**liposome** composition for delivery of nucleic acid)

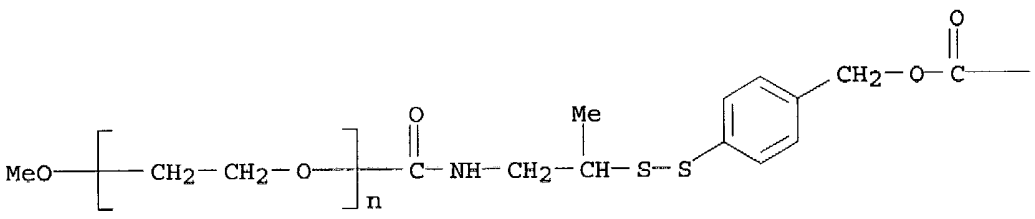
IT 304013-12-5P **304013-20-5P** 495399-43-4P 495399-45-6P 495399-46-7P 495399-47-8P 495399-51-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**liposome** composition for delivery of nucleic acid)

IT 495399-44-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**liposome** composition for delivery of nucleic acid)

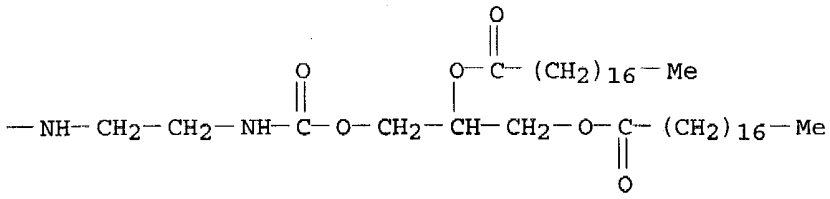
IT **495399-53-6P**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**liposome** composition for delivery of nucleic acid)

RN 495399-53-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[3,8,14-trioxo-11-[(1-oxooctadecyl)oxy]-2,9,13-trioxa-4,7-diazahentriacont-1-yl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A

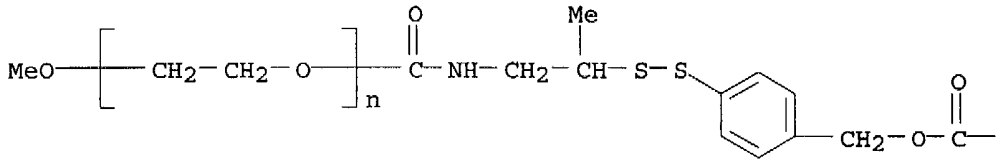


PAGE 1-B

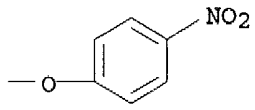


IT **304013-20-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**liposome** composition for delivery of nucleic acid)
RN 304013-20-5 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L14 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692666 HCAPLUS
DOCUMENT NUMBER: 138:373961
TITLE: Reversible PEGylation: thiolytic regeneration of active protein from its polymer conjugates
AUTHOR(S): Zalipsky, Samuel; Kiwan, Radwan; Mullah, Nasreen
CORPORATE SOURCE: ALZA Corp., Mountain View, CA, 94043, USA
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 953-954. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB To overcome the problems associated with PEGylation, a new linking chemical designed to produce gradual in vivo loss of polyethylene glycol (PEG) chains from their conjugates is introduced. Just as a promoiety of a

prodrug, PEG would be present in these reversible conjugates only temporarily, improving such characteristics as pharmacokinetics and biodistribution. The initial results of using lysozyme and cysteine as models of a protein and a cleaving agent, resp., are presented. The reversible PEGylation approach is based on the benzyl carbamate para-substituted with a disulfide (dithiobenzyl, DTB) linker. Thiolytic scission of the disulfide results in unstable p-thiobenzyl urethane, which spontaneously decomps. via 1,6-elimination, regenerating the original amino group of the protein. The results demonstrate that the simple thiol, cysteine, ubiquitously found in physiol. environments, is an effective cleaving agent of PEG-DTB-protein. MPEG-DTB-lysozyme cleanly reverts to the native protein, with concomitant recovery of the activity, which had been initially lost due to the PEGylation. Thus, regeneration of the native protein as the key requirement of reversible PEGylation has been demonstrated.

CC 63-5 (Pharmaceuticals)

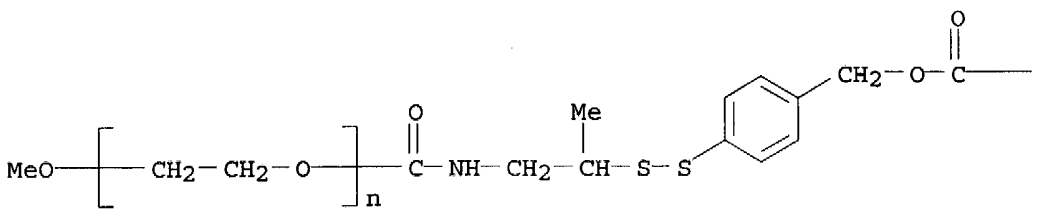
IT **522630-43-9D**, protein conjugates
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cleavage of PEG-protein conjugate by cysteine)

IT **522630-43-9D**, protein conjugates
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cleavage of PEG-protein conjugate by cysteine)

RN 522630-43-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[(aminocarbonyl)oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— NH_2

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:625021 HCAPLUS
DOCUMENT NUMBER: 137:353475
TITLE: Reversible, dithiobenzyl urethane linked polymer-protein conjugates
AUTHOR(S): Zalipsky, Samuel; Kiwan, Radwan; Mullah, Nasreen
CORPORATE SOURCE: Alza Corporation, Mountain View, CA, 94043, USA
SOURCE: Polymer Preprints (American Chemical Society, Division

of Polymer Chemistry) (2002), 43(2), 693-694
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: English

AB Attachment of methoxy-poly(ethylene glycol) (mPEG) to protein amino groups via dithiobenzyl (DTB) carbamate linkage results in a conjugate capable of losing its PEG coating by reacting with thiols (e.g., Cys). A new reagent, mPEG-DTB-NPC, was prepared and evaluated on a model protein, lysozyme. Thiolytic decomposition of mPEG-DTB-lysozyme lead to recovery of the original protein (by LC-MS) concomitantly with its bacterial cell-wall lysing activity. The results suggest suitability of this approach for temporary PEGylation of therapeutic proteins, which dramatically lose their activity when subjected to permanent PEGylation. Since scission of accessible disulfides under in vivo conditions is known, we anticipate the mPEG-DTB-proteins to behave as macromol. prodrugs.

CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 34, 63

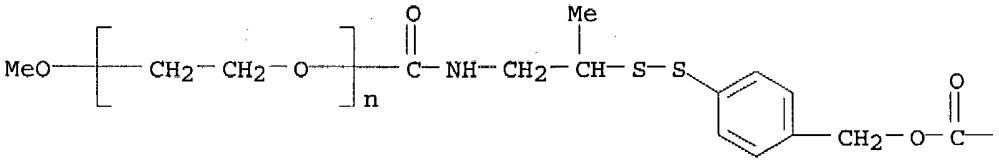
IT 124661-64-9DP, reaction product with lysozyme **304013-20-5DP**, reaction product with lysozyme
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(reversible, dithiobenzyl urethane linked polymer-protein conjugates)

IT **304013-20-5DP**, reaction product with lysozyme
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(reversible, dithiobenzyl urethane linked polymer-protein conjugates)

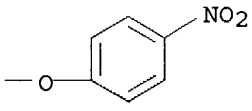
RN 304013-20-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:350561 HCAPLUS
DOCUMENT NUMBER: 138:112286
TITLE: New approach to gene delivery mediated by reversible PEGylation of cationic lipid-DNA complexes

AUTHOR(S): Zalipsky, S.; Quinn, Y.; Jin, B.; Zhang, W.; Engbers, C.; Mullah, N.; Kiwan, R.; Huang, S. K.

CORPORATE SOURCE: ALZA Corporation, Mountain View, CA, 94043, USA

SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1177-1178. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Reversible PEGylation can temporarily shield a DNA-lipid complex and then unmask it at a later stage, either before or after internalization by cells. This new approach provides increased control over the extent of the biol. cell transfection / expression of the loaded DNA, with important implications for potential systemic gene delivery.

CC 63-6 (Pharmaceuticals)

IT Drug delivery systems
(**liposomes**; gene delivery mediated by reversible PEGylation of cationic lipid-DNA complexes)

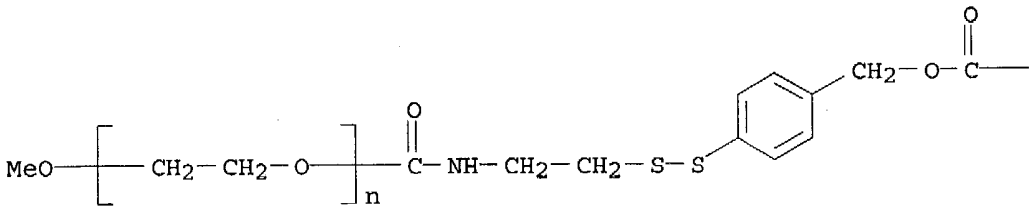
IT **304013-02-3D**, complexes with DNA **304013-04-5D**, complexes with DNA
RL: FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(gene delivery mediated by reversible PEGylation of cationic lipid-DNA complexes)

IT **304013-02-3D**, complexes with DNA **304013-04-5D**, complexes with DNA
RL: FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(gene delivery mediated by reversible PEGylation of cationic lipid-DNA complexes)

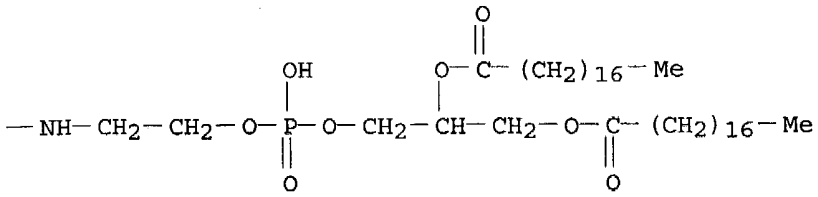
RN 304013-02-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-yl]phenyl]dithio]ethyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A

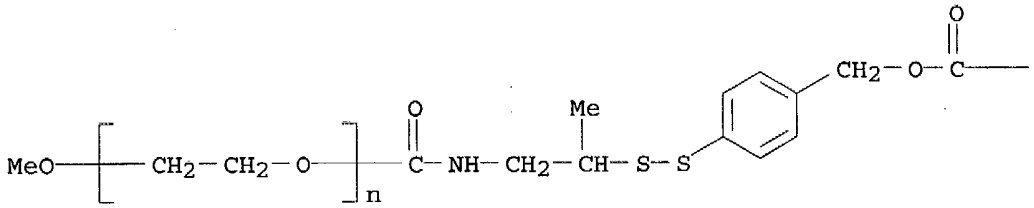


PAGE 1-B

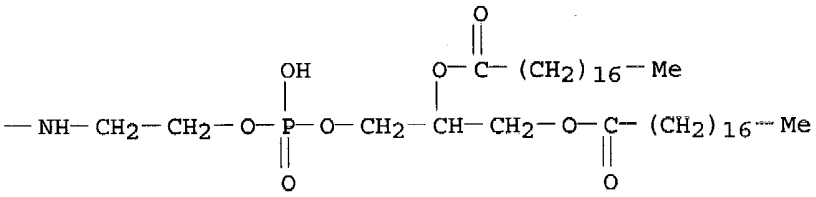


RN 304013-04-5 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-yl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



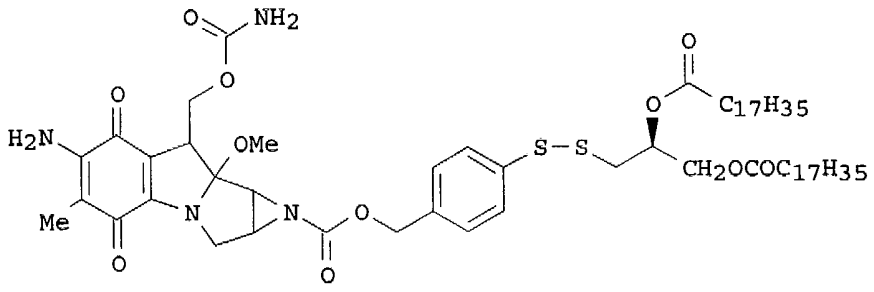
PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:346931 HCAPLUS
DOCUMENT NUMBER: 138:112129
TITLE: New **liposomal** prodrug of mitomycin C
AUTHOR(S): Zalipsky, S.; Kiwan, R.; Qazen, M.; Flaherty, T.; Engbers, C.; Guo, L.; Zomorodi, K.; Feng, W.; Yeh, J.; Horowitz, A.; Indap, M.; Gabizon, A.
CORPORATE SOURCE: ALZA Corporation, Mountain View, CA, 94043, USA
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 437-438. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8

DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I

AB A new prodrug-conjugate (I), containing 1,2-diacyl lipid as a promoiety linked to mitomycin C (MMC) via thiolytically-cleavable dithiobenzyl carbamate, was prepared and evaluated in STEALTH **liposomes**. The **liposomal** prodrug had much lower cytotoxicity, which was recovered by cysteine-mediated MMC release. In vivo the prodrug was well retained in long-circulating **liposomes**, and was more tumor inhibitory than MMC in tumor-bearing mice. Thus, this approach appears to offer an improved delivery system for MMC.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 26

ST mitomycin C prodrug **liposome**

IT Antitumor agents
Dissolution
(**liposomal** prodrug of mitomycin C)

IT Drug delivery systems
(**liposomes**; **liposomal** prodrug of mitomycin C)

IT Drug delivery systems
(prodrugs; **liposomal** prodrug of mitomycin C)

IT 50-07-7, Mitomycin c
RL: PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(**liposomal** prodrug of mitomycin C)

IT **303983-00-8P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**liposomal** prodrug of mitomycin C)

IT 53339-53-0, p-Mercaptobenzyl alcohol 111662-21-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(**liposomal** prodrug of mitomycin C)

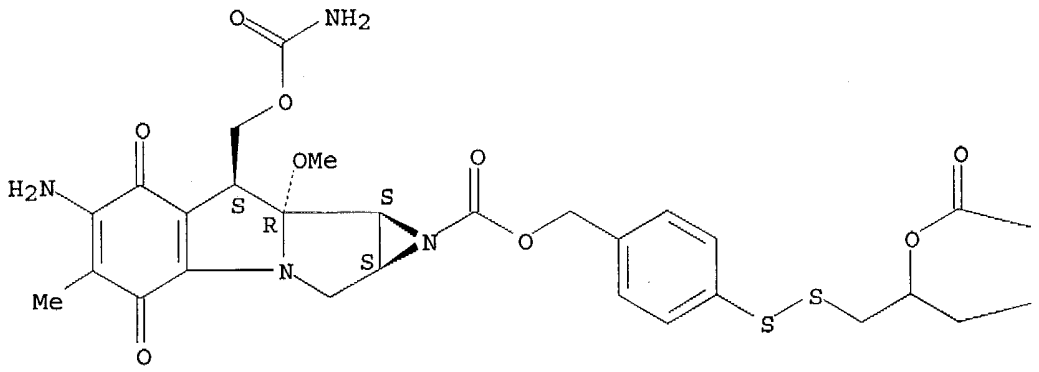
IT **303983-00-8P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**liposomal** prodrug of mitomycin C)

RN 303983-00-8 HCAPLUS

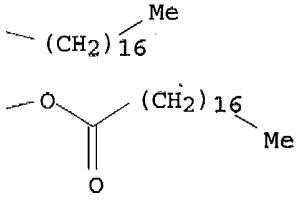
CN Azirino[2',3':3,4]pyrrolo[1,2-a]indole-1(2H)-carboxylic acid, 6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxo-, [4-[[2,3-bis[(1-oxooctadecyl)oxy]propyl]dithio]phenyl]methyl ester, (1aS,8S,8aR,8bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:346626 HCAPLUS
DOCUMENT NUMBER: 138:95428
TITLE: Polymer-protein conjugates as macromolecular prodrugs: Reversible pegylation of proteins
AUTHOR(S): Zalipsky, S.; Mullah, N.; Kiwan, R.
CORPORATE SOURCE: ALZA Corporation, Mountain View, CA, 94043, USA
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 73-74. Controlled Release Society: Minneapolis, Minn. CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Attachment of polyethylene glycol to amino groups on a protein via dithiobenzyl carbamate linkage results in a conjugate capable of losing

its PEG coating by reacting with thiols (e.g. Cys). The conjugate decomposition leads to recovery of the original protein concomitantly with its biol. activity. Lysozyme was evaluated as a model protein. The results suggest suitability of this approach for temporary PEGylation of therapeutic proteins, which dramatically lose their activity when subjected to permanent PEGylation.

CC 63-6 (Pharmaceuticals)

IT **304013-20-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reversible pegylation of proteins in polymer-protein conjugates as macromol. prodrugs)

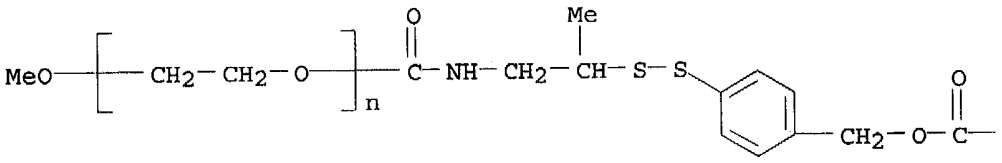
IT **304013-20-5D**, conjugates with proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reversible pegylation of proteins in polymer-protein conjugates as macromol. prodrugs)

IT **304013-20-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reversible pegylation of proteins in polymer-protein conjugates as macromol. prodrugs)

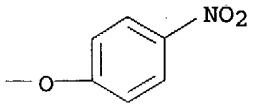
RN 304013-20-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

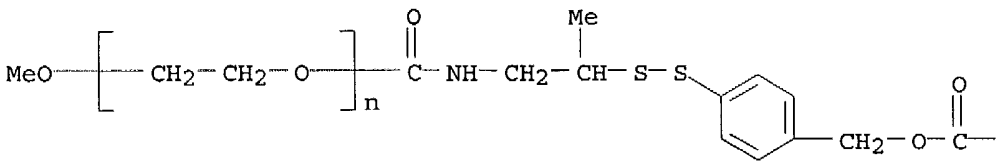


IT **304013-20-5D**, conjugates with proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reversible pegylation of proteins in polymer-protein conjugates as macromol. prodrugs)

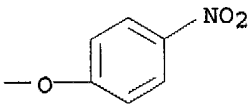
RN 304013-20-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:380438 HCAPLUS
DOCUMENT NUMBER: 135:24657
TITLE: Selective cellular targeting: multifunctional delivery vehicles
INVENTOR(S): Glazier, Arnold
PATENT ASSIGNEE(S): Drug Innovation & Design, Inc., USA
SOURCE: PCT Int. Appl., 981 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036003	A2	20010525	WO 2000-US31262	20001114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001016075	A5	20010530	AU 2001-16075	20001114
EP 1255567	A1	20021113	EP 2000-978631	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003138432	A1	20030724	US 2000-738625	20001215

PRIORITY APPLN. INFO.:
US 1999-165485P P 19991115
US 2000-239478P P 20001011
US 2000-241937P P 20001020
WO 2000-US31262 W 20001114
US 2000-712465 B1 20001115

AB The present invention relates to the compns., methods, and applications of

a novel approach to selective cellular targeting. The purpose of this invention is to enable the selective delivery and/or selective activation of effector mols. to target cells for diagnostic or therapeutic purposes. The present invention relates to multi-functional prodrugs or targeting vehicles wherein each functionality is capable of enhancing targeting selectivity, affinity, intracellular transport, activation or detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for cancer treatment.

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 8, 15, 25, 28

IT 23214-92-8DP, immucillin G derivs. 209799-75-7DP, doxorubicin derivs.
341549-52-8P 341549-53-9P **341549-71-1P** 341549-87-9P
341552-14-5P 341552-35-0P 341552-87-2P 341553-15-9P 341553-47-7P
341553-59-1P 341990-79-2P 341990-80-5P 341990-94-1P 341990-96-3P
341990-98-5P 341990-99-6P 341991-00-2P 342383-78-2P
342384-75-2P 342385-42-6P 342388-64-1P 342389-43-9P 342389-44-0P
342389-46-2P 342389-61-1P 342389-62-2P 342389-66-6P 342389-71-3P
342389-73-5P 342389-75-7P 342389-76-8P 342390-71-0P 342391-02-0P
342391-78-0P 342392-24-9P 342392-67-0P 342392-75-0P 342392-76-1P
342392-79-4P 342392-80-7P 342395-29-3P 342395-30-6P 342395-36-2P
342395-37-3P 342395-39-5P 342395-40-8P 342395-41-9P 342395-43-1P
342395-44-2P 342395-69-1P 342395-75-9P 342395-77-1P 342395-78-2P
342395-79-3P 342395-81-7P 342395-84-0P 342395-85-1P 342395-95-3P
342396-15-0P 342396-56-9P 342397-18-6P 342397-65-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT 1194-98-5P 1499-29-2P 6974-29-4P 51819-63-7P 90359-20-9P
138915-62-5P 147281-71-8P 165172-57-6P 165454-06-8P 177575-34-7P
214532-01-1P 216220-13-2P 240428-96-0P 341549-88-0P 341549-89-1P
341549-90-4P 341549-91-5P 341549-92-6P 341549-93-7P 341549-94-8P
341549-95-9P **341549-96-0P** **341549-97-1P**
341549-98-2P 341549-99-3P 341550-00-3P 341550-01-4P 341550-02-5P
341550-03-6P 341550-04-7P 341550-05-8P 341550-06-9P 341550-07-0P
341550-08-1P 341550-09-2P 341550-10-5P 341550-11-6P 341550-12-7P
341550-13-8P 341550-14-9P 341550-15-0P 341550-16-1P 341550-17-2P
341550-18-3P 341550-19-4P 341550-20-7P 341550-21-8P
341550-22-9P 341550-23-0P 341550-24-1P 341550-25-2P 341550-26-3P
341550-27-4P 341550-28-5P 341550-29-6P 341550-30-9P 341550-31-0P
341550-32-1P 341550-33-2P 341550-34-3P 341550-35-4P 341550-36-5P
341550-37-6P 341550-38-7P 341550-39-8P 341550-40-1P 341550-41-2P
341550-42-3P 341550-43-4P 341550-44-5P 341550-45-6P 341550-46-7P
341550-47-8P 341550-48-9P 341550-49-0P 341550-50-3P 341550-51-4P
341550-52-5P 341550-53-6P 341550-54-7P 341550-55-8P 341550-56-9P
341550-57-0P 341550-58-1P 341550-59-2P 341550-60-5P 341550-61-6P
341550-62-7P 341550-63-8P 341550-64-9P 341550-65-0P 341550-66-1P
341550-67-2P 341550-68-3P 341550-69-4P 341550-70-7P 341550-71-8P
341550-72-9P 341550-73-0P 341550-74-1P 341550-75-2P 341550-76-3P
341550-77-4P 341550-78-5P 341550-79-6P 341550-80-9P 341550-81-0P
341550-82-1P 341550-83-2P 341550-84-3P 341550-85-4P 341550-86-5P
341550-87-6P 341550-88-7P 341550-89-8P 341550-90-1P 341550-91-2P
341550-92-3P 341550-93-4P 341550-94-5P 341550-95-6P 341550-96-7P
341550-97-8P 341550-98-9P 341550-99-0P 341551-00-6P 341551-01-7P
341551-02-8P 341551-03-9P 341551-04-0P 341551-05-1P 341551-06-2P
341551-07-3P 341551-08-4P 341551-09-5P 341551-10-8P 341551-11-9P

341551-12-0P 341551-14-2P 341551-16-4P 341551-17-5P 341551-18-6P
341551-19-7P 341551-20-0P 341551-21-1P 341551-22-2P 341551-23-3P
341551-24-4P 341551-25-5P 341551-26-6P 341551-27-7P 341551-28-8P
341551-29-9P 341551-30-2P 341551-31-3P 341551-32-4P 341551-33-5P
341551-34-6P 341551-35-7P 341551-36-8P **341551-37-9P**
341551-38-0P 341551-39-1P 341551-40-4P 341551-41-5P 341551-42-6P
341551-43-7P 341551-44-8P 341551-45-9P 341551-46-0P 341551-47-1P
341551-48-2P 341551-49-3P 341551-50-6P 341551-51-7P 341551-51-7P
341551-52-8P 341551-53-9P 341551-54-0P 341551-55-1P 341551-56-2P
341551-57-3P 341551-58-4P 341551-59-5P 341551-60-8P 341551-61-9P
341551-62-0P 341551-63-1P 341551-64-2P 341551-65-3P 341551-67-5P
341551-68-6P 341551-69-7P 341551-70-0P 341551-71-1P 341551-72-2P
341551-73-3P 341551-74-4P 341551-75-5P **341551-76-6P**
341551-77-7P 341551-78-8P 341551-79-9P 341551-80-2P 341551-81-3P
341551-82-4P 341551-83-5P 341551-84-6P 341551-85-7P
341551-86-8P 341551-87-9P 341551-88-0P 341551-89-1P
341551-90-4P 341551-91-5P 341551-92-6P 341551-93-7P 341551-94-8P
341551-95-9P 341551-96-0P 341551-97-1P 341551-98-2P 341551-99-3P
341552-00-9P 341552-01-0P 341552-02-1P 341552-03-2P 341552-04-3P
341552-05-4P 341552-06-5P 341552-07-6P 341552-08-7P 341552-09-8P
341552-10-1P
RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT 341552-11-2P 341552-12-3P 341552-13-4P 341552-15-6P 341552-16-7P
341552-17-8P 341552-18-9P 341552-19-0P 341552-20-3P 341552-21-4P
341552-22-5P 341552-23-6P 341552-24-7P 341552-25-8P 341552-26-9P
341552-27-0P 341552-28-1P 341552-29-2P 341552-30-5P 341552-31-6P
341552-32-7P 341552-33-8P 341552-34-9P 341552-36-1P 341552-37-2P
341552-38-3P 341552-39-4P 341552-40-7P 341552-41-8P 341552-42-9P
341552-43-0P 341552-44-1P 341552-45-2P 341552-46-3P 341552-47-4P
341552-48-5P 341552-49-6P 341552-50-9P 341552-51-0P 341552-52-1P
341552-53-2P 341552-54-3P 341552-55-4P 341552-56-5P 341552-57-6P
341552-58-7P 341552-59-8P 341552-60-1P 341552-61-2P 341552-62-3P
341552-63-4P **341552-64-5P** 341552-65-6P 341552-66-7P
341552-67-8P 341552-68-9P 341552-69-0P 341552-70-3P 341552-71-4P
341552-72-5P 341552-73-6P 341552-74-7P 341552-75-8P 341552-76-9P
341552-77-0P 341552-78-1P 341552-79-2P 341552-80-5P 341552-81-6P
341552-82-7P 341552-83-8P 341552-84-9P 341552-85-0P 341552-86-1P
341552-88-3P 341552-89-4P 341552-90-7P 341552-91-8P 341552-93-0P
341552-94-1P 341552-95-2P 341552-96-3P 341552-97-4P 341552-98-5P
341552-99-6P 341553-00-2P 341553-01-3P 341553-02-4P 341553-03-5P
341553-04-6P 341553-05-7P 341553-06-8P 341553-07-9P 341553-08-0P
341553-09-1P 341553-10-4P 341553-11-5P 341553-12-6P 341553-13-7P
341553-14-8P 341553-16-0P 341553-17-1P 341553-18-2P 341553-19-3P
341553-20-6P 341553-21-7P 341553-22-8P 341553-23-9P 341553-24-0P
341553-25-1P 341553-26-2P 341553-27-3P 341553-28-4P 341553-29-5P
341553-30-8P 341553-31-9P 341553-32-0P 341553-33-1P 341553-34-2P
341553-35-3P **341553-36-4P** 341553-37-5P **341553-38-6P**
341553-39-7P 341553-40-0P 341553-41-1P **341553-42-2P**
341553-43-3P 341553-45-5P 341553-46-6P 341553-48-8P 341553-49-9P
341553-50-2P 341553-51-3P 341553-52-4P 341553-53-5P 341553-54-6P
341553-55-7P 341553-56-8P 341553-57-9P 341553-58-0P 341553-60-4P
341553-61-5P 341553-62-6P 341553-63-7P 341553-64-8P 341553-65-9P
341553-67-1P 341553-68-2P **341553-69-3P** 341553-70-6P
341990-72-5P 341990-73-6P 341990-74-7P 341990-75-8P 341990-76-9P
341990-77-0P 341990-82-7P 341990-83-8P 341990-84-9P

341990-85-0P 341990-86-1P 341990-87-2P 341990-88-3P 341990-89-4P
341990-90-7P 341990-91-8P 341990-92-9P
341990-93-0P 341990-95-2P 341990-97-4P 341991-01-3P
342393-40-2P 342395-76-0P 342395-83-9P 342395-94-2P 342398-29-2P
RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

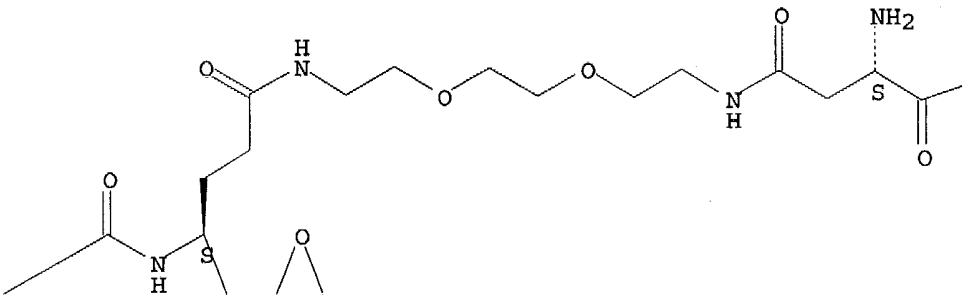
IT 197245-25-3P 341549-54-0P 341549-55-1P **341549-56-2P**
341549-57-3P 341549-58-4P **341549-59-5P** 341549-60-8P
341549-61-9P 341549-62-0P 341549-63-1P 341549-74-4P 341549-76-6P
341549-78-8P 341549-79-9P 341549-80-2P 341549-81-3P 341549-82-4P
341549-83-5P 341549-84-6P 341549-85-7P 341549-86-8P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

IT **341549-52-8P 341549-71-1P 341990-98-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

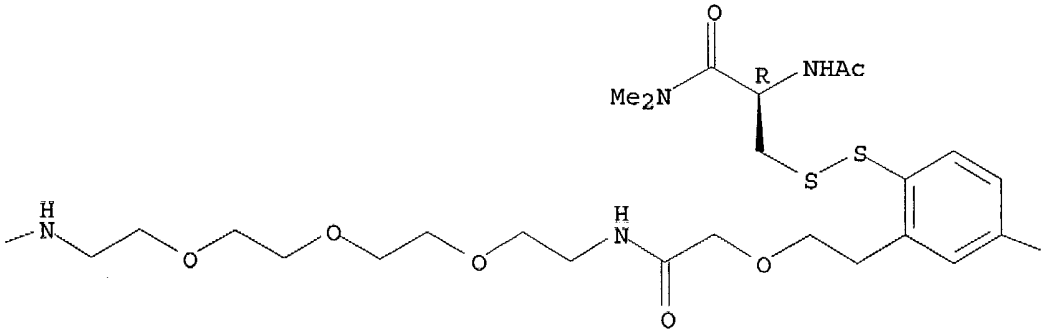
RN 341549-52-8 HCAPLUS
CN Butanedioic acid, [[5-[[[[[4-[(3S,19S)-19-amino-38-[2-[[(2R)-2-(acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[[[[(2E)-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-1-oxo-1H-inden-7-yl]amino]carbonyl]oxy]methyl]phenyl]-3-[(9H-fluoren-9-ylmethoxy)carbonyl]-1,6,17,20,34-pentaoxo-10,13,24,27,30,36-hexaoxa-2,7,16,21,33-pentaazaoctatriacont-1-yl]phenyl][(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

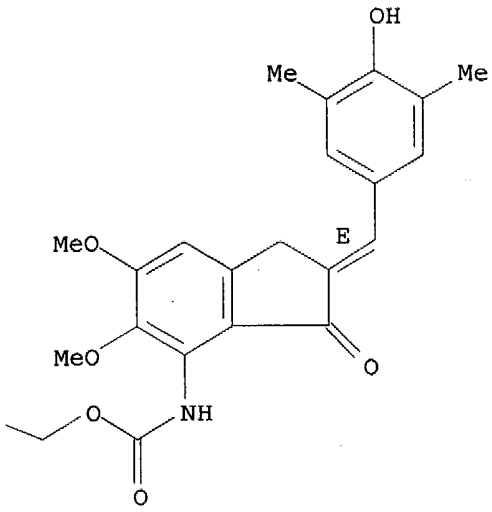
PAGE 1-B



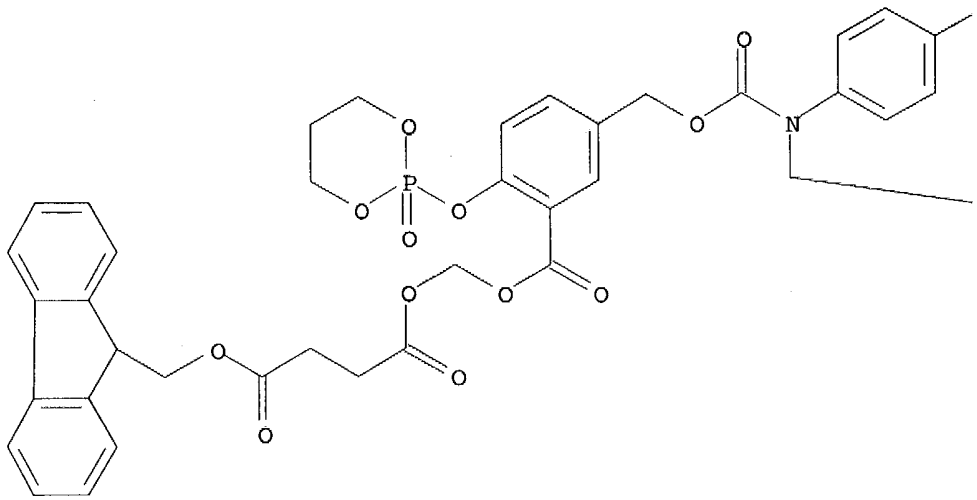
PAGE 1-C



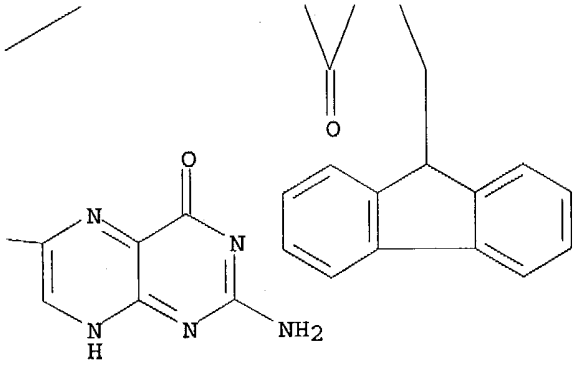
PAGE 1-D



PAGE 2-A



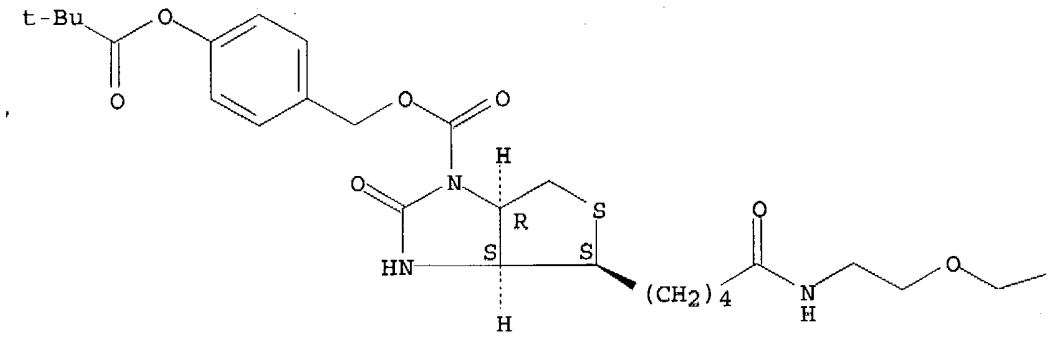
PAGE 2-B



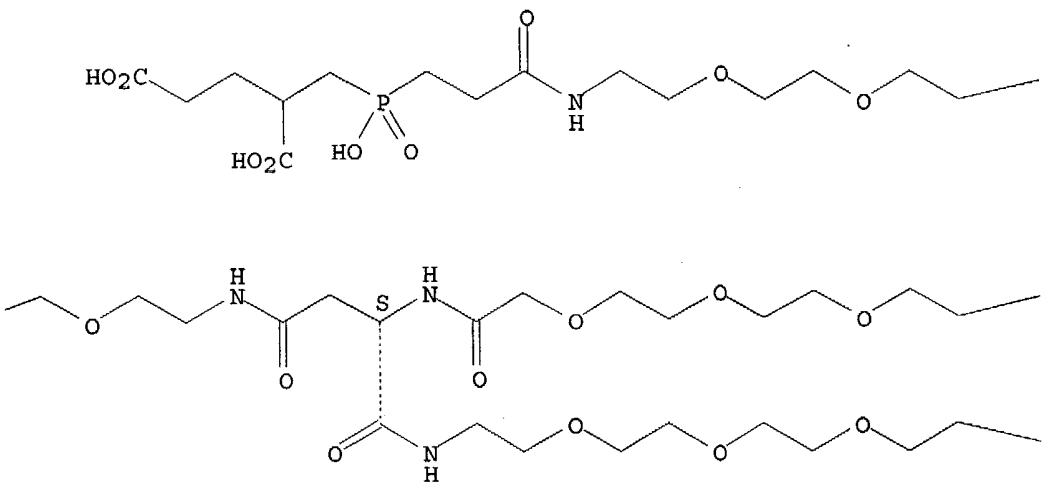
RN 341549-71-1 HCAPLUS
CN L-Argininamide, N2-[(16S)-35-[2-[[(2R)-2-(acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[[[[(2E)-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-3-oxo-1H-inden-4-yl]amino]carbonyl]oxy]methyl]phenyl]-16-[17-[(3aS,4S,6aR)-1-[[[4-(2,2-dimethyl-1-oxopropoxy)phenyl]methoxy]carbonyl]hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-2,13-dioxo-6,9-dioxa-3,12-diazaheptadec-1-yl]-1,14,17,31-tetraoxo-3,6,9,12,21,24,27,33-octaoxa-15,18,30-triazapentatriacont-1-yl]-N-[18,20-dicarboxy-16-hydroxy-16-oxido-13-oxo-3,6,9-trioxa-12-aza-16-phosphaeicos-1-yl]-L-asparaginyl-3-[2-[2-(2-aminoethoxy)ethoxy]ethoxy]propanoyl-L-tyrosyl-L-isoleucylglycyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

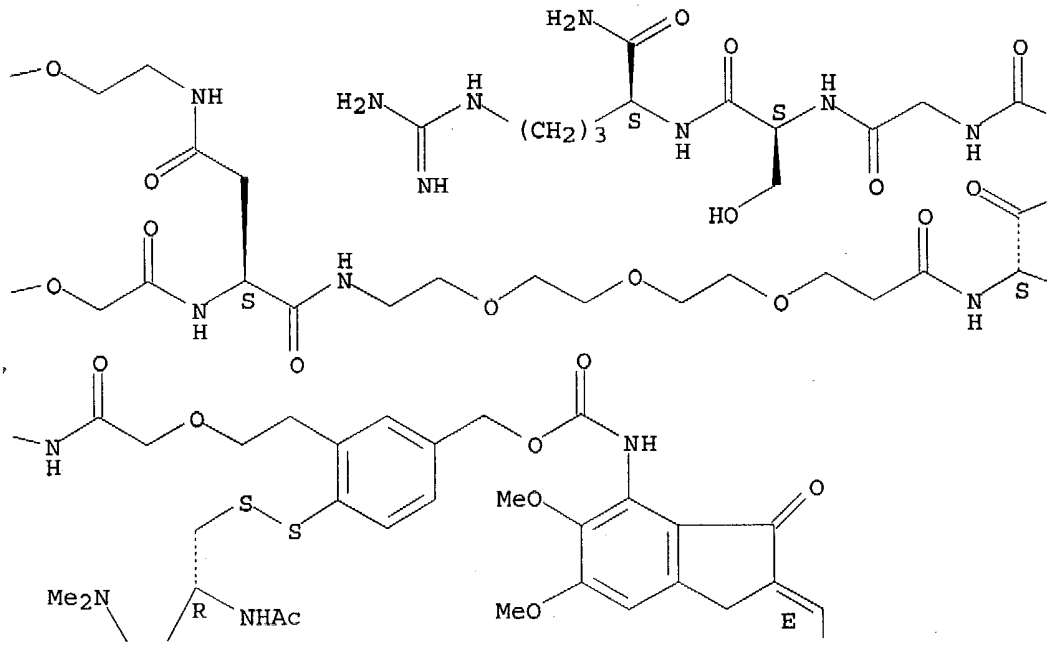
PAGE 1-A



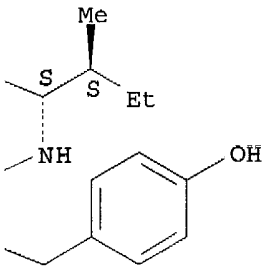
PAGE 1-B



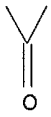
PAGE 1-C

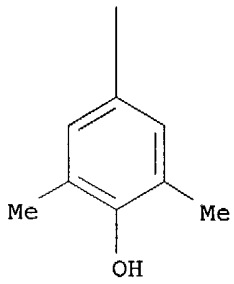


PAGE 1-D



PAGE 2-C



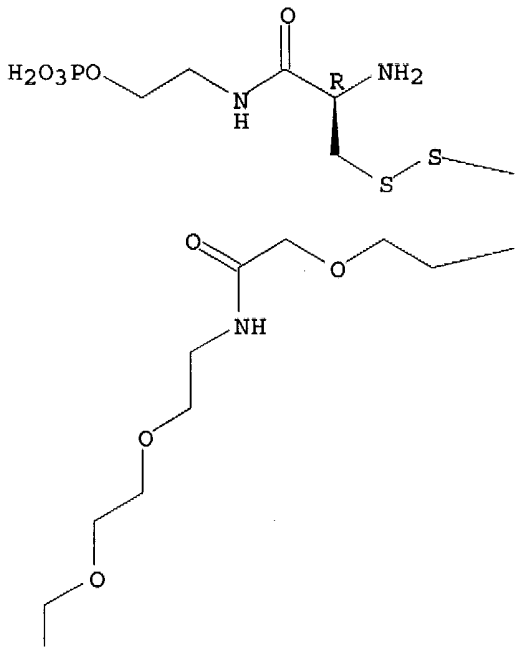


RN 341990-98-5 HCAPLUS

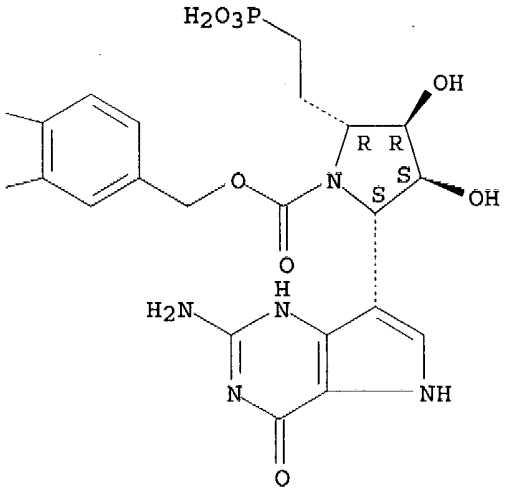
CN 7,10,13,19,22,25,28,34,37,40-Decaoxa-4,16,31,43-tetraazaoctatetracontan-48-oic acid, 47-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][[[3-[[2-(dimethylamino)-2-oxoethoxy]carbonyl]-4-[[5-(phosphonooxy)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]phenyl]methoxy]carbonyl]amino]benzoyl]amino]-31-[17-[5-[[[[(2S,3S,4R,5R)-2-(2-amino-4,5-dihydro-4-oxo-1H-pyrrolo[3,2-d]pyrimidin-7-yl)-3,4-dihydroxy-5-(2-phosphonoethyl)-1-pyrrolidinyl]carbonyl]oxy]methyl]-2-[[(2R)-2-amino-3-oxo-3-[[2-(phosphonooxy)ethyl]amino]propyl]dithio]phenyl]-13-oxo-3,6,9,15-tetraoxa-12-azaheptadec-1-yl]-1-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-16-[15-[4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-4-[(hydroxyamino)carbonyl]-2H-pyran-2-yl]-13-oxo-3,6,9-trioxa-12-azapentadec-1-yl]-3,17,30,44-tetraoxo-, (47S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

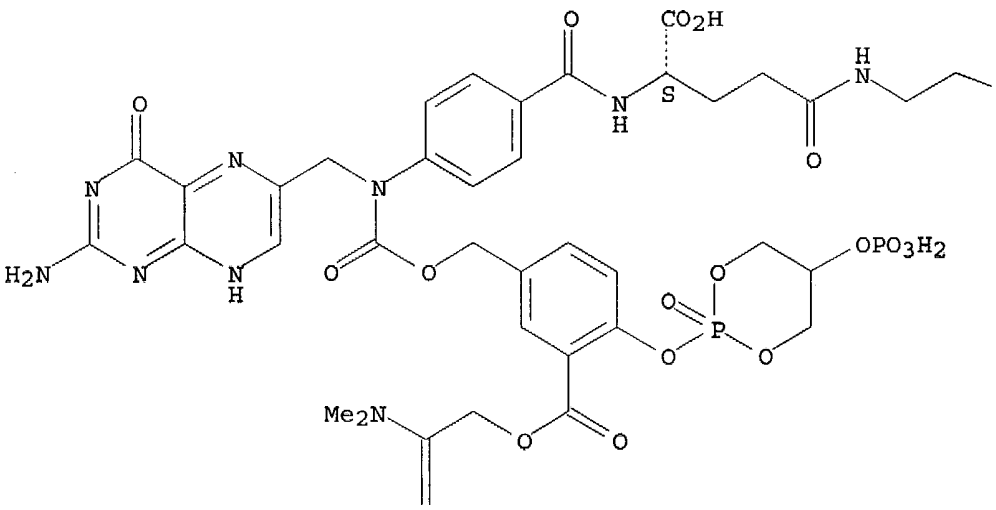
PAGE 1-B



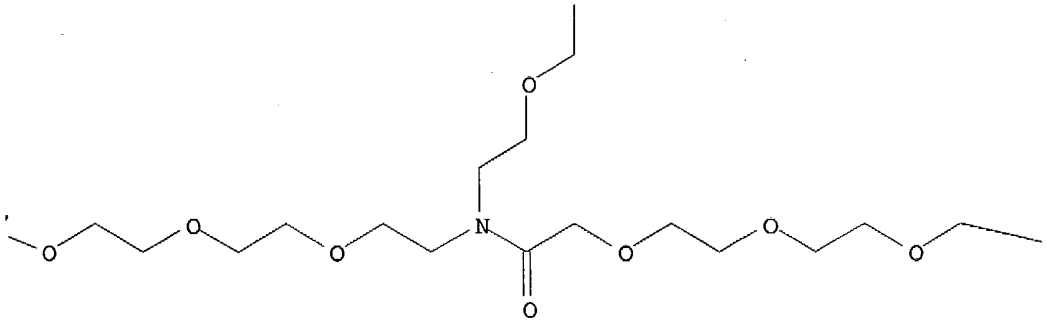
PAGE 1-C



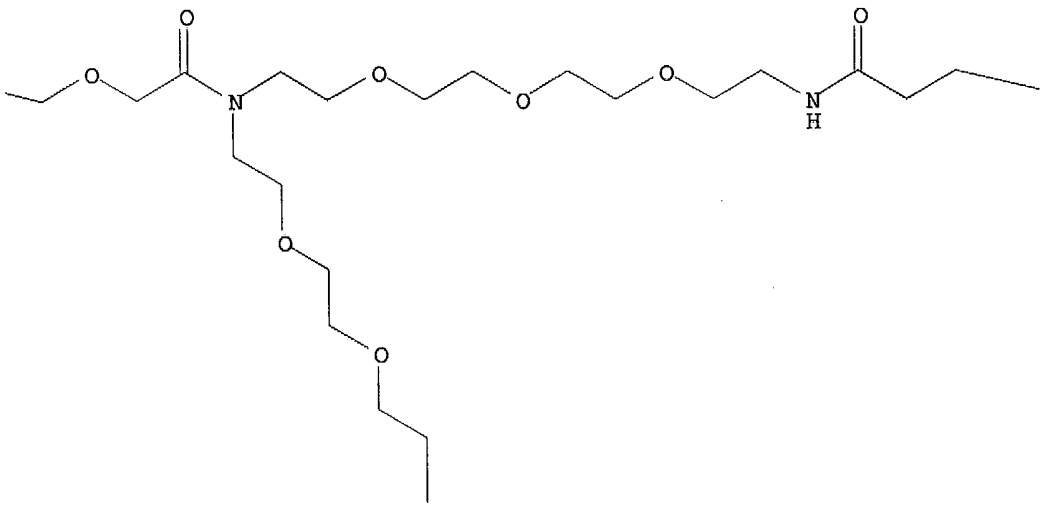
PAGE 2-A



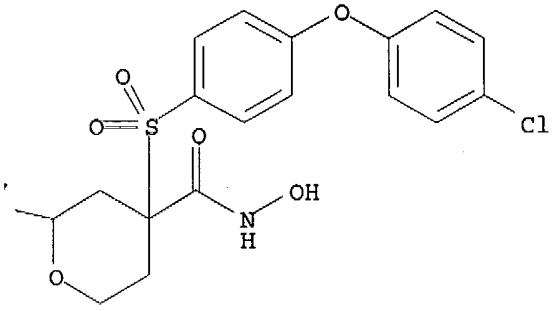
PAGE 2-B



PAGE 2-C

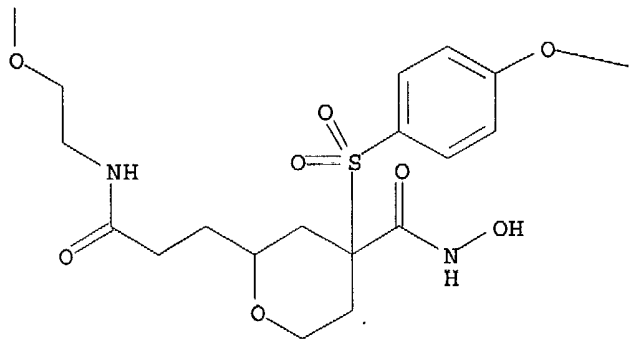


PAGE 2-D

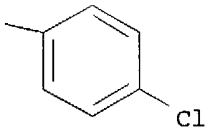


PAGE 3-A

PAGE 3-C



PAGE 3-D



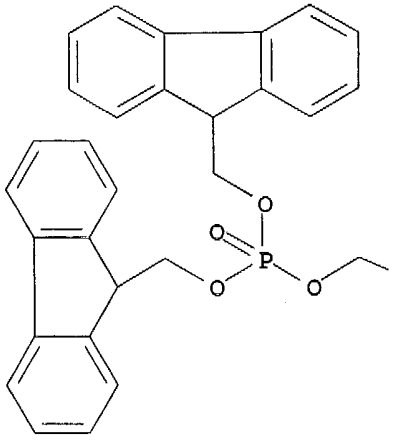
IT **341549-95-9P 341549-96-0P 341549-97-1P**
341550-18-3P 341551-34-6P 341551-37-9P
341551-76-6P 341551-82-4P 341551-86-8P
341552-64-5P 341553-36-4P 341553-38-6P
341553-42-2P 341553-69-3P 341990-77-0P
341990-90-7P 341990-91-8P 341990-93-0P
RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

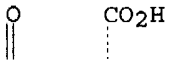
RN 341549-95-9 HCAPLUS

CN Butanedioic acid, [[5-[[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][4-[(3S)-3-carboxy-33-[2-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-yl]dithio]-5-[[[[[3-[[3-[(9-methoxy-5,11-dimethyl-6H-pyrido[4,3-b]carbazol-1-yl)amino]propyl]methylamino]propyl]amino]carbonyl]oxy]methyl]phenyl]-1,6,29-trioxo-10,13,16,22,25,31-hexaoxa-2,7,19,28-tetraazatritriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

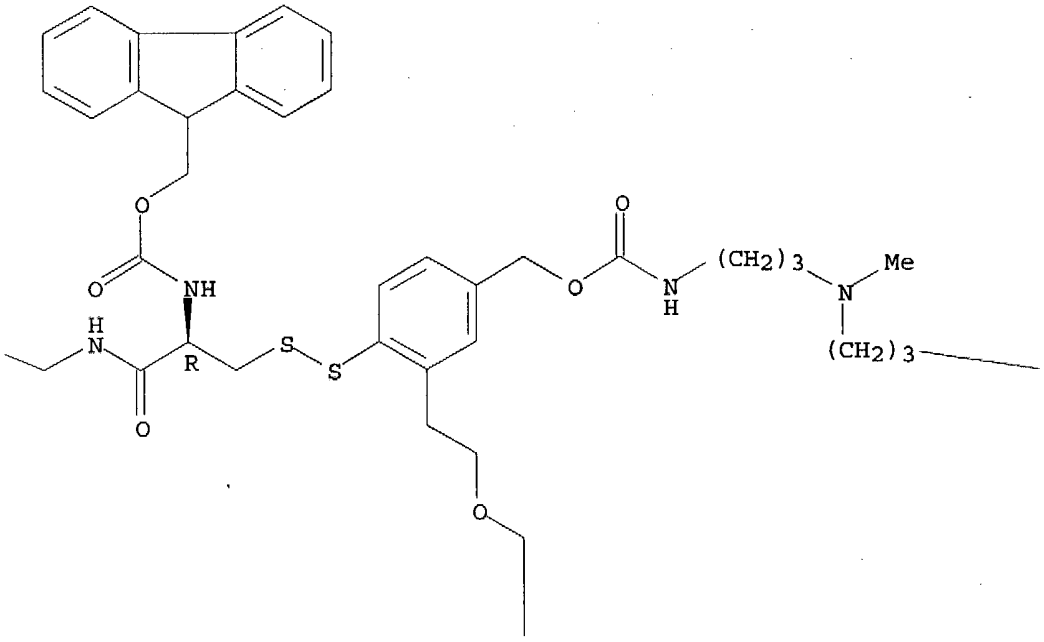
Absolute stereochemistry.

PAGE 1-B

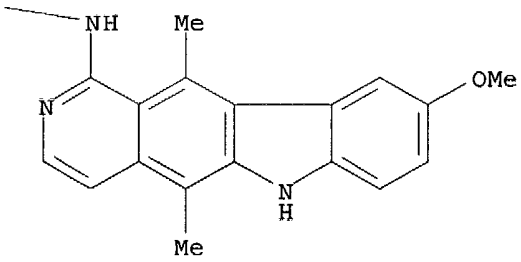




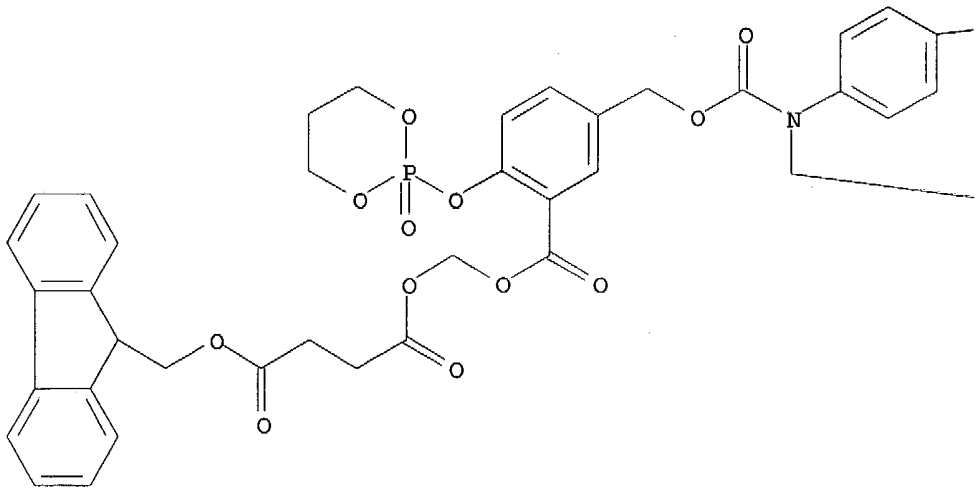
PAGE 1-C



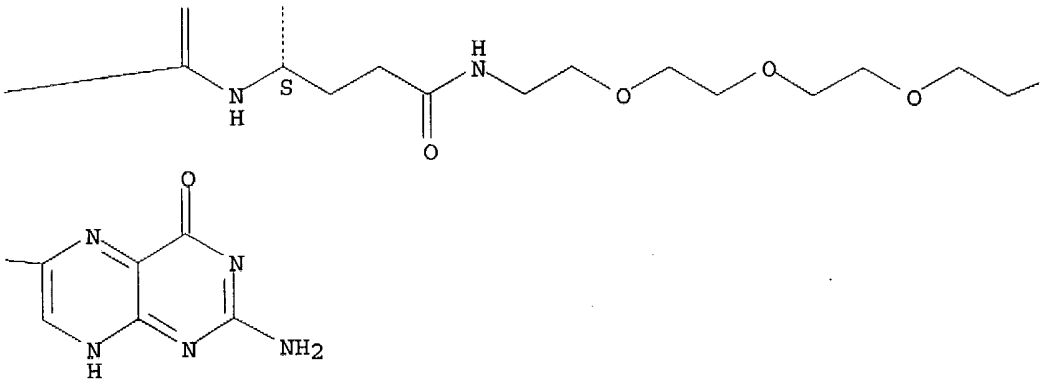
PAGE 1-D



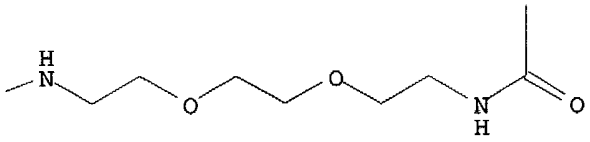
PAGE 2-A



PAGE 2-B



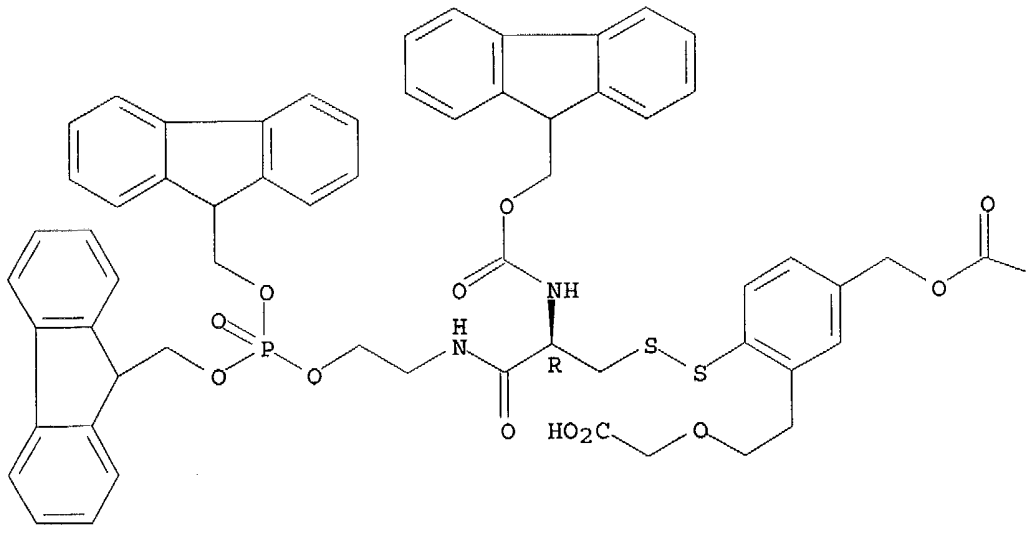
PAGE 2-C

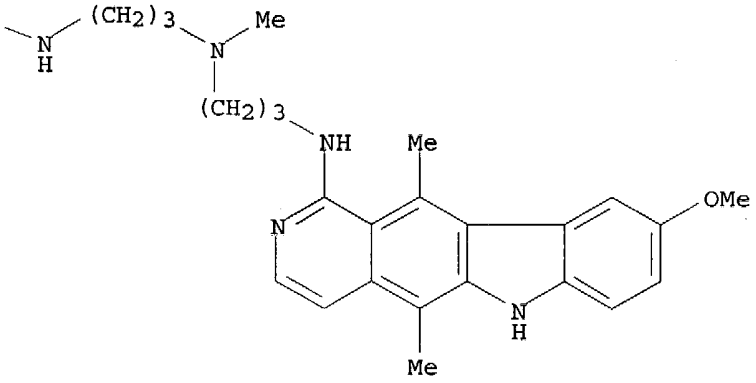


RN 341549-96-0 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[2-[2-(carboxymethoxy)ethyl]-4-[[[[[3-[[3-[(9-methoxy-5,11-dimethyl-6H-pyrido[4,3-b]carbazol-1-yl)amino]propyl]methylamino]propyl]amino]carbonyl]oxy]methyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 11-(9H-fluoren-9-ylmethyl) ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

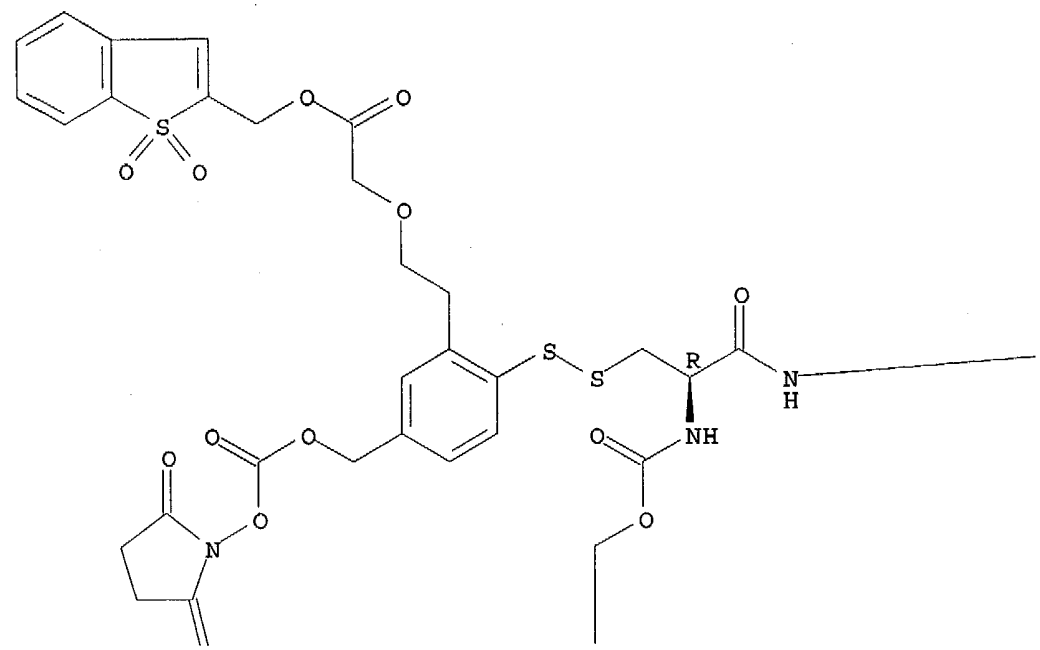




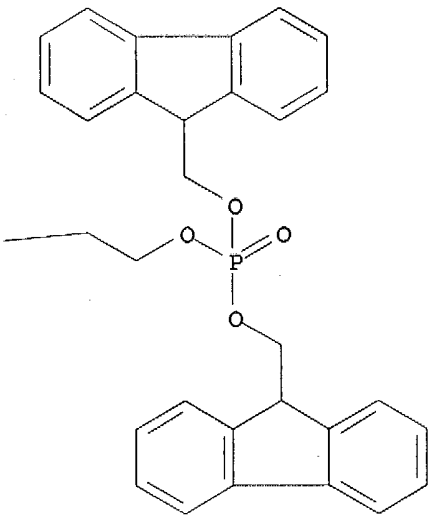
RN 341549-97-1 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[2-[2-[2-[(1,1-dioxidobenzo[b]thien-2-yl)methoxy]-2-oxoethoxy]ethyl]-4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 9H-fluoren-9-ylmethyl ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

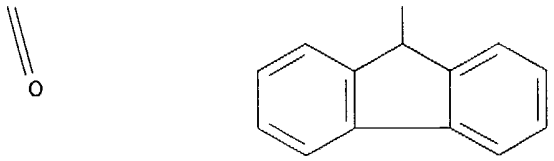
PAGE 1-A



PAGE 1-B



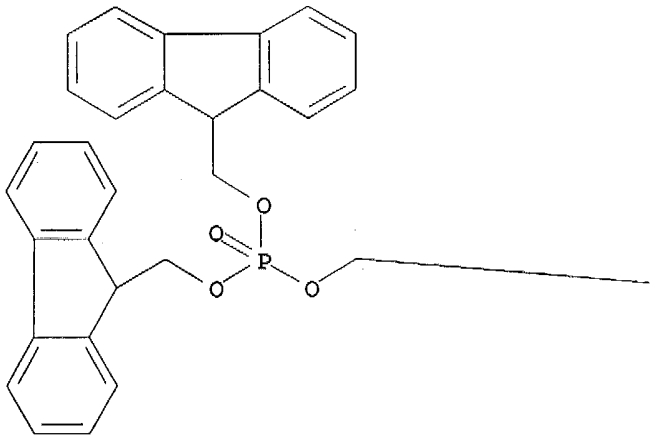
PAGE 2-A



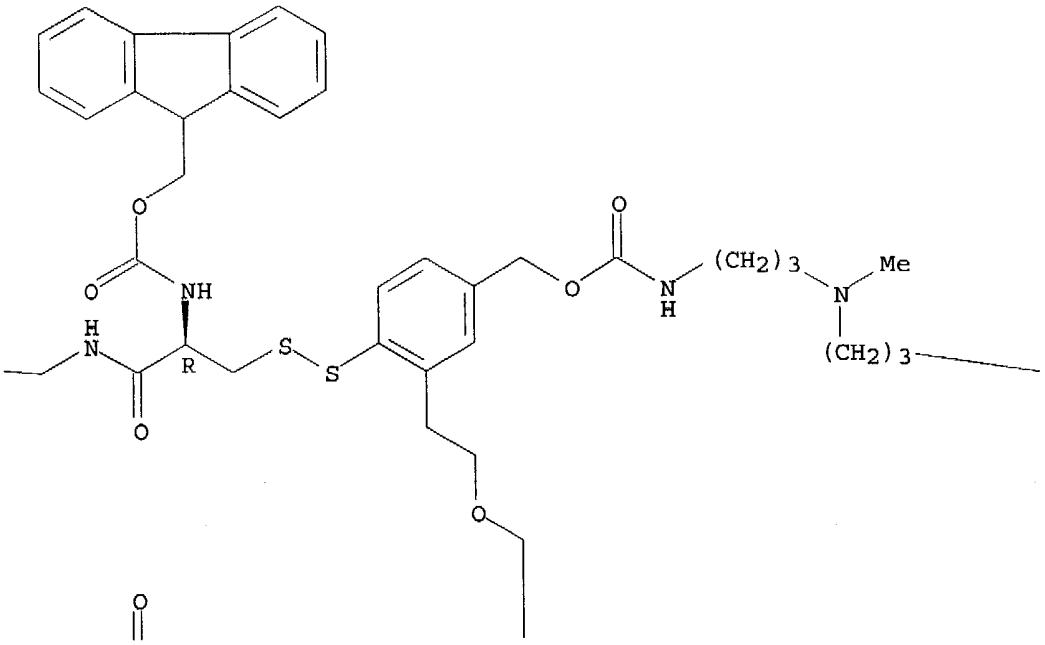
RN 341550-18-3 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[2-[15-[3-[2-(carboxymethoxy)ethyl]-4-[[[4-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-2,2-dimethylbutoxy]sulfonyl]oxy]phenyl]-5,13-dioxo-3,9-dioxa-6,12-diazapentadec-1-yl]-4-[[[[[3-[[3-[(9-methoxy-5,11-dimethyl-6H-pyrido[4,3-b]carbazol-1-yl)amino]propyl]methylamino]propyl]amino]carbonyl]oxy]methyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 11-(9H-fluoren-9-ylmethyl) ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

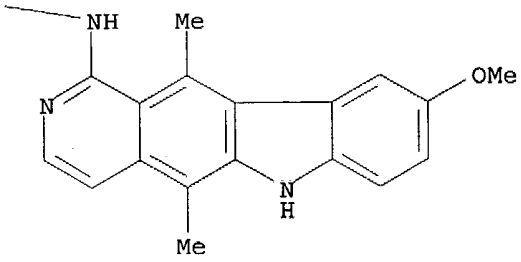
PAGE 1-A



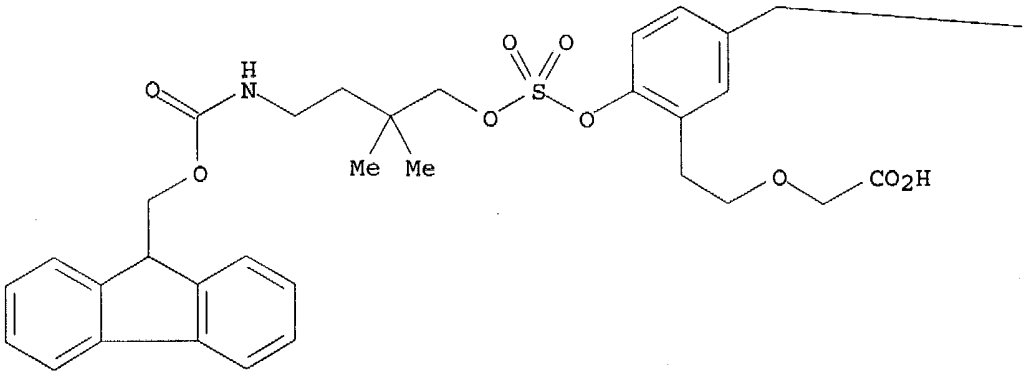
PAGE 1-B



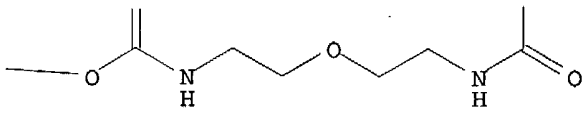
PAGE 1-C



PAGE 2-A



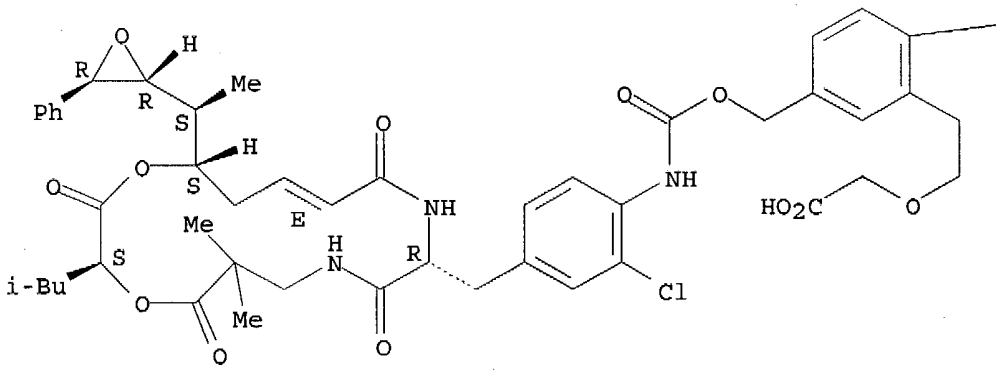
PAGE 2-B



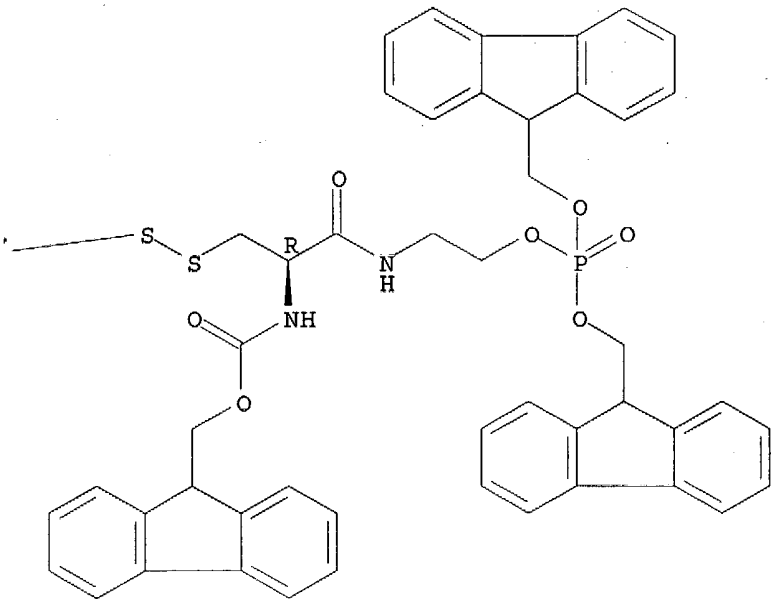
RN 341551-34-6 HCAPLUS
CN Cyclo[2,2-dimethyl-β-alanyl-(2S)-2-hydroxy-4-methylpentanoyl-(2E,5S,6S)-5-hydroxy-6-[(2R,3R)-3-phenyloxiranyl]-2-heptenoyl-4-[[[[3-[2-(carboxymethoxy)ethyl]-4-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-yl]dithio]phenyl]methoxy]carbonyl]amino]-3-chloro-D-phenylalanyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



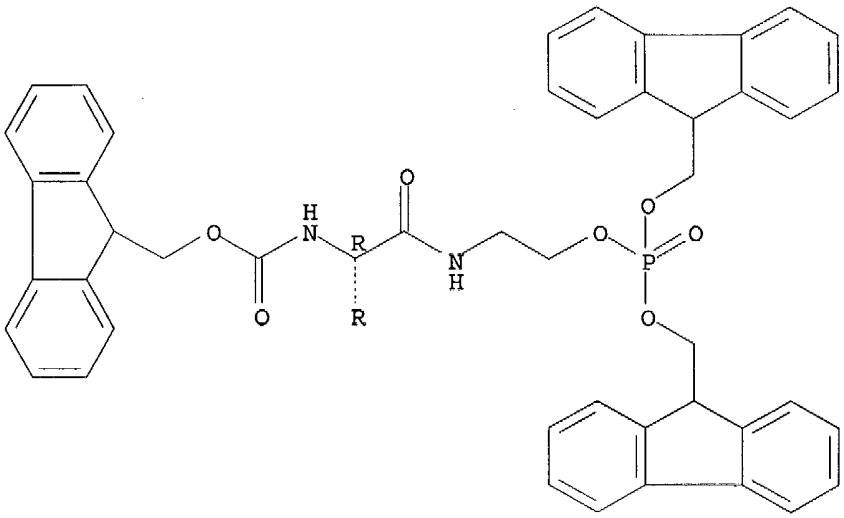
PAGE 1-B



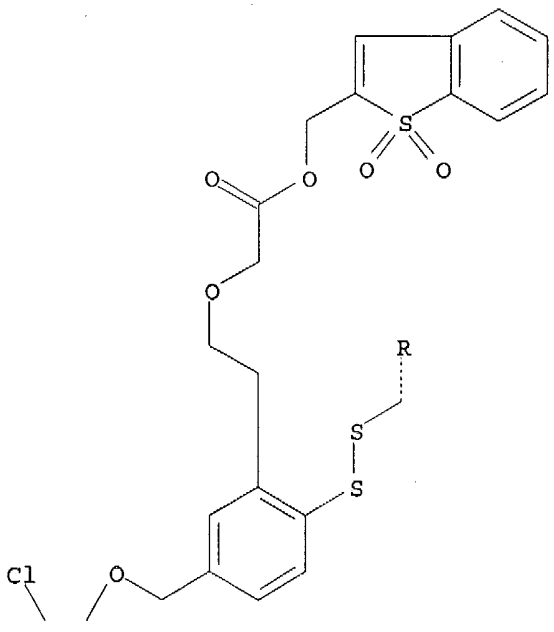
RN 341551-37-9 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[4-[[(chlorocarbonyl)oxy]methyl]-2-[2-[2-[(1,1-dioxidobenzo[b]thien-2-yl)methoxy]-2-oxoethoxy]ethyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 9H-fluoren-9-ylmethyl ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

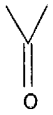
PAGE 1-A



PAGE 2-A



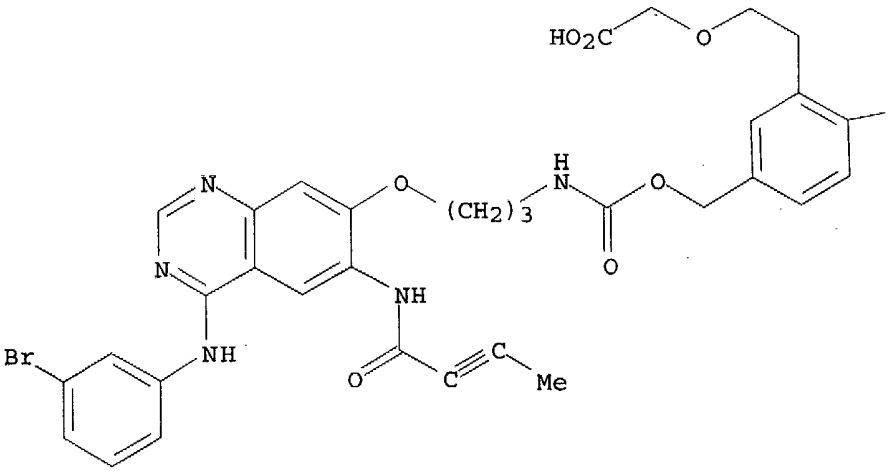
PAGE 3-A



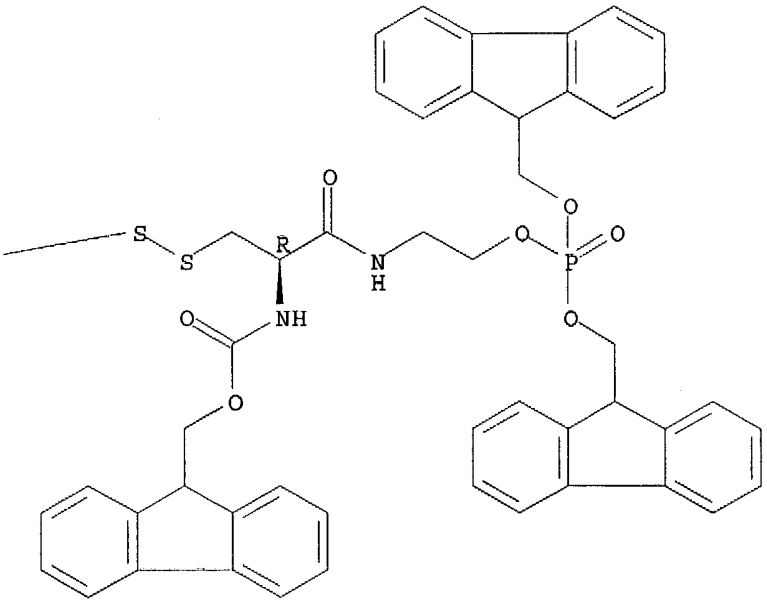
RN 341551-76-6 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[4-[[[[[3-[[4-[(3-bromophenyl)amino]-6-[(1-oxo-2-butynyl)amino]-7-quinazolinyl]oxy]propyl]amino]carbonyl]oxy]methyl]-2-[2-(carboxymethoxy)ethyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 11-(9H-fluoren-9-ylmethyl) ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

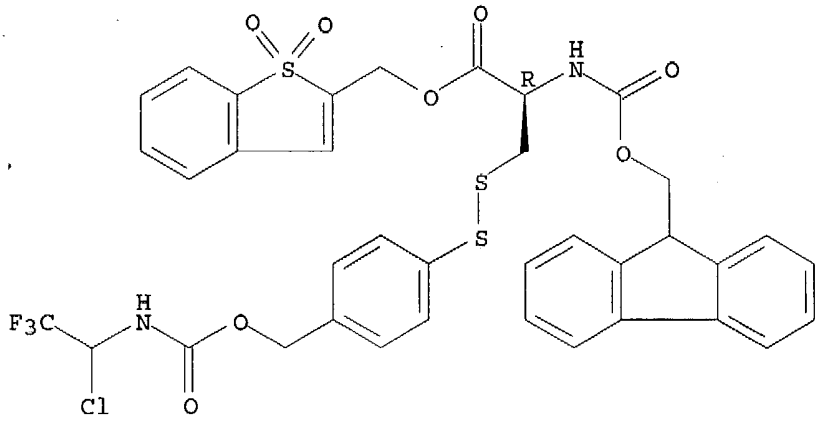


PAGE 1-B



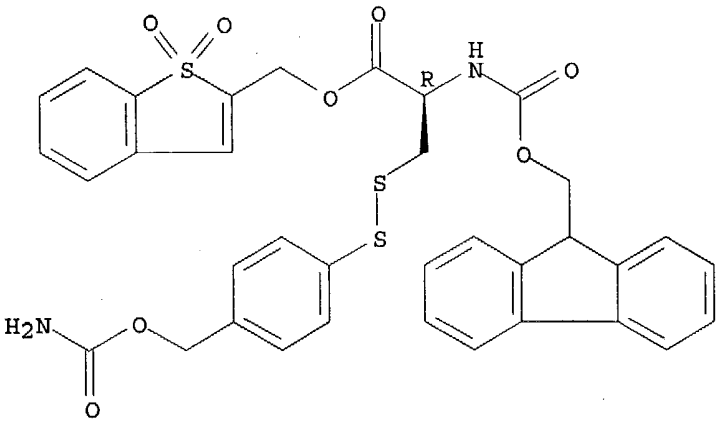
RN 341551-82-4 HCAPLUS
CN L-Alanine, 3-[[4-[[[[(1-chloro-2,2,2-trifluoroethyl)amino]carbonyl]oxy]methyl]phenyl]dithio]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-, (1,1-dioxidobenzo[b]thien-2-yl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



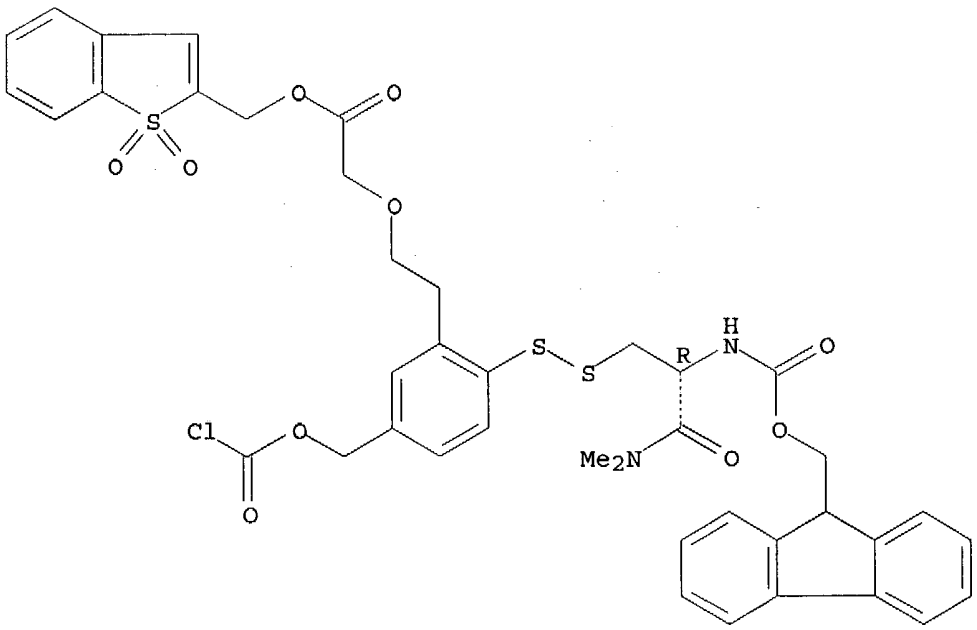
RN 341551-86-8 HCAPLUS
CN L-Alanine, 3-[[4-[[(aminocarbonyl)oxy]methyl]phenyl]dithio]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-, (1,1-dioxidobenzo[b]thien-2-yl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



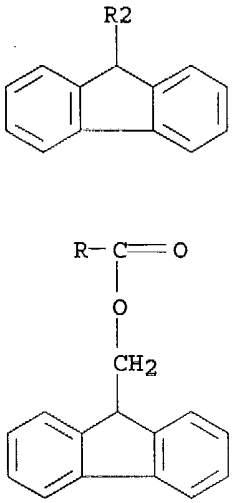
RN 341552-64-5 HCAPLUS
CN Acetic acid, [2-[5-[[(chlorocarbonyl)oxy]methyl]-2-[[(2R)-3-(dimethylamino)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-3-oxopropyl]dithio]phenyl]ethoxy]-, (1,1-dioxidobenzo[b]thien-2-yl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

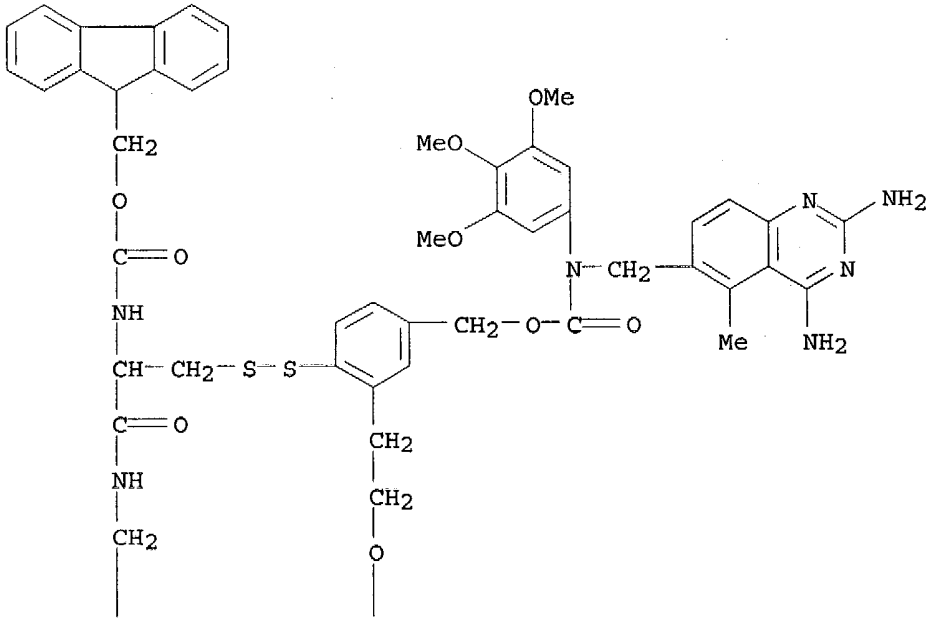


RN 341553-36-4 HCAPLUS
CN Butanedioic acid, mono[[[5-[[[[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl][4-[(3S)-36-[5-[[[[[(2,4-diamino-5-methyl-6-quinazolinyl)methyl](3,4,5-trimethoxyphenyl)amino]carbonyl]oxy]methyl]-2-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-yl]dithio]phenyl]-3-[(9H-fluoren-9-ylmethoxy)carbonyl]-1,6,32-trioxo-10,13,16,22,25,28,34-heptaoxa-2,7,19,31-tetraazahexatriacont-1-yl]phenyl]amino]carbonyl]oxy]methyl]-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl] ester (9CI) (CA INDEX NAME)

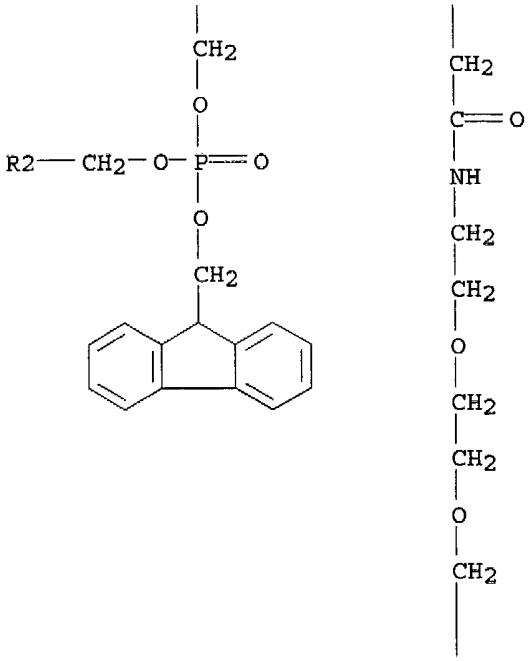
PAGE 1-A



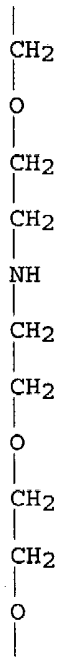
PAGE 2-A



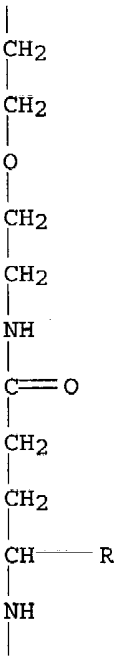
PAGE 3-A



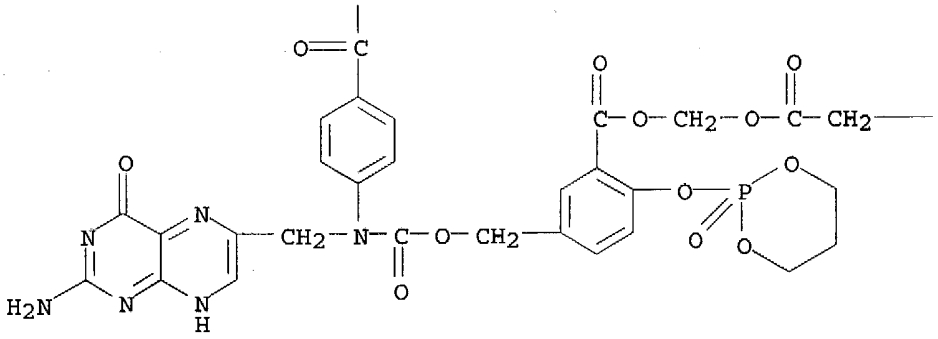
PAGE 4-A



PAGE 5-A



PAGE 6-A



PAGE 6-B

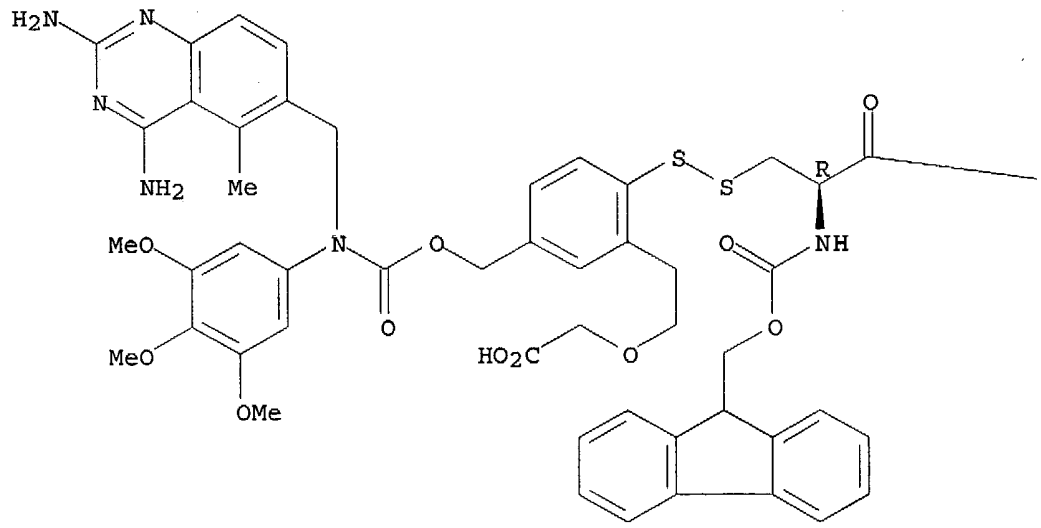
— CH_2 — CO_2H

RN 341553-38-6 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[2-[2-(carboxymethoxy)ethyl]-4-[[[[[(2,4-diamino-5-methyl-6-quinazolinyl)methyl](3,4,5-trimethoxyphenyl)amino]carbonyl]oxy]methyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-,

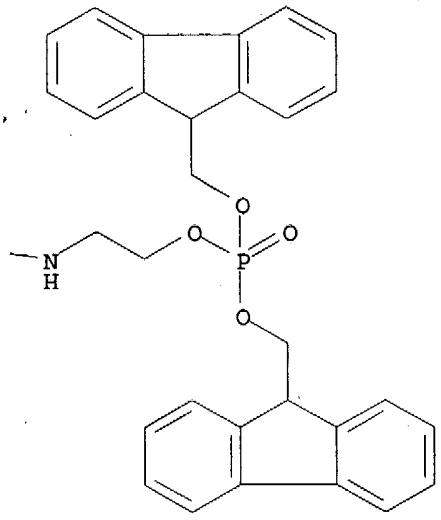
11-(9H-fluoren-9-ylmethyl) ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



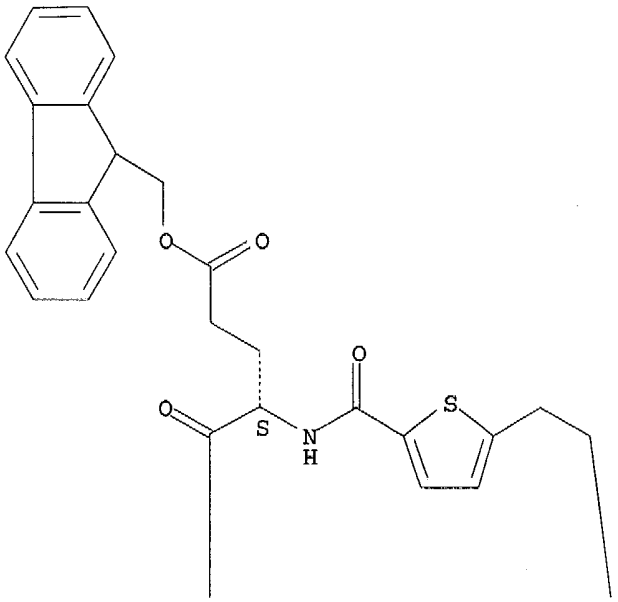
RN 341553-42-2 HCAPLUS

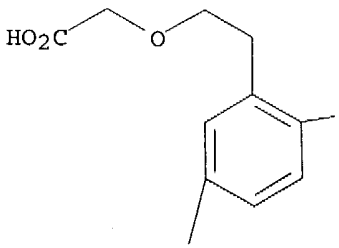
CN L-Glutamic acid, N-[[5-[2-[2-amino-8-[[[3-[2-(carboxymethoxy)ethyl]-4-[[(2R)-10-(9H-fluoren-9-yl)-8-(9H-fluoren-9-ylmethoxy)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-8-oxido-3-oxo-7,9-dioxa-4-aza-8-phosphadec-1-yl]dithio]phenyl]methoxy]carbonyl]-4,6,7,8-tetrahydro-4-oxo-1H-

pyrimido[5,4-b][1,4]thiazin-6-yl]ethyl]-2-thienyl]carbonyl]-,
1,5-bis(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

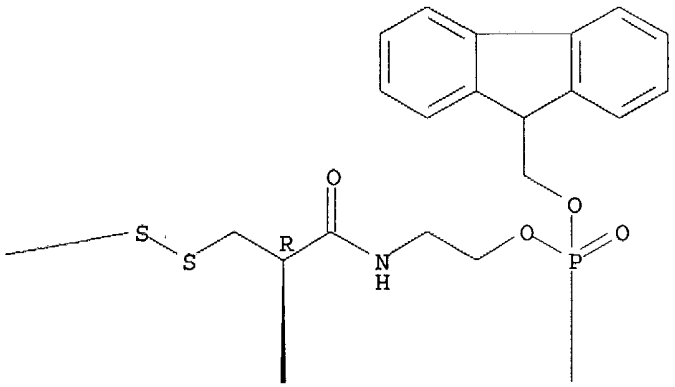
Absolute stereochemistry.

PAGE 1-A

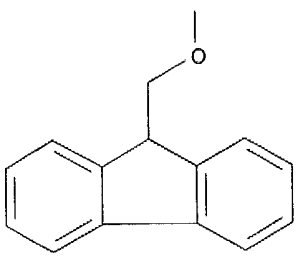


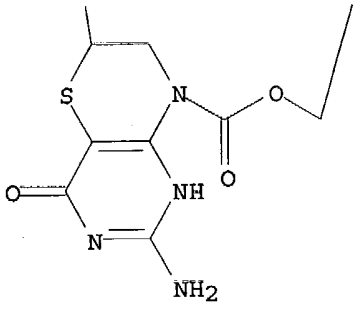


PAGE 1-B

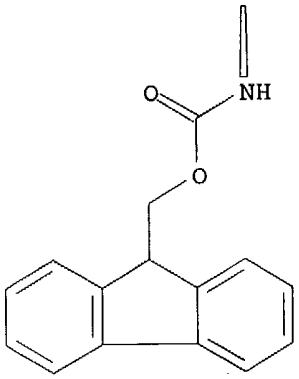


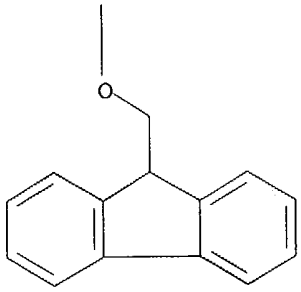
PAGE 2-A





PAGE 2-B

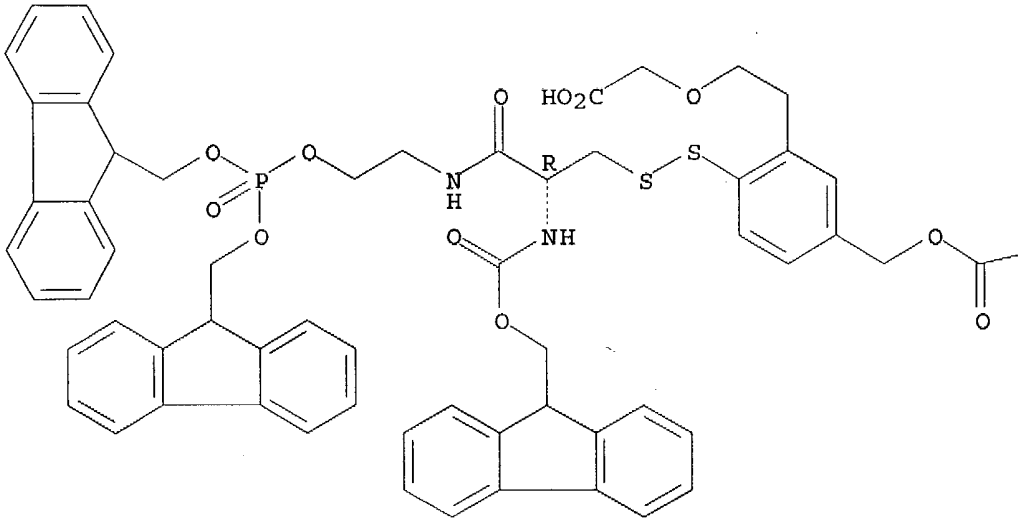




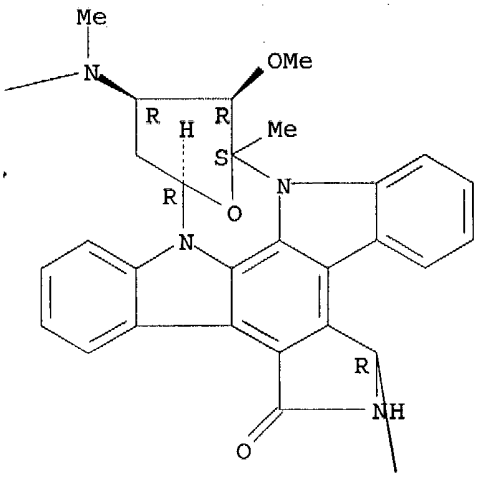
RN 341553-69-3 HCAPLUS
CN 2,4-Dioxa-7,10-diaza-3-phosphaundecan-11-oic acid, 9-[[[4-[[[[[(3R,9S,10R,11R,13R)-3-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2,3,10,11,12,13-hexahydro-9-methyl-10-methoxy-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]methylamino]carbonyl]oxy]methyl]-2-[2-(carboxymethoxy)ethyl]phenyl]dithio]methyl]-1-(9H-fluoren-9-yl)-3-(9H-fluoren-9-ylmethoxy)-8-oxo-, 11-(9H-fluoren-9-ylmethyl) ester, 3-oxide, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

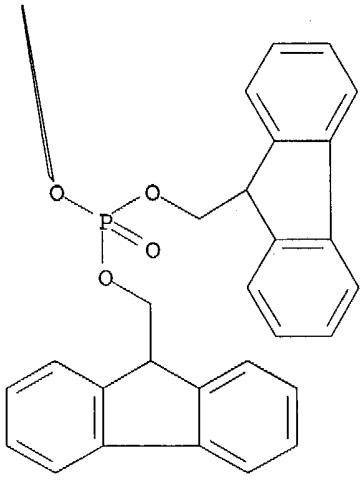
PAGE 1-A



PAGE 1-B



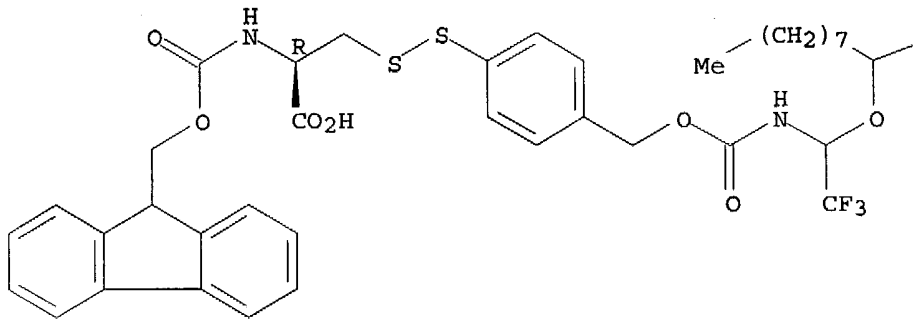
PAGE 2-B



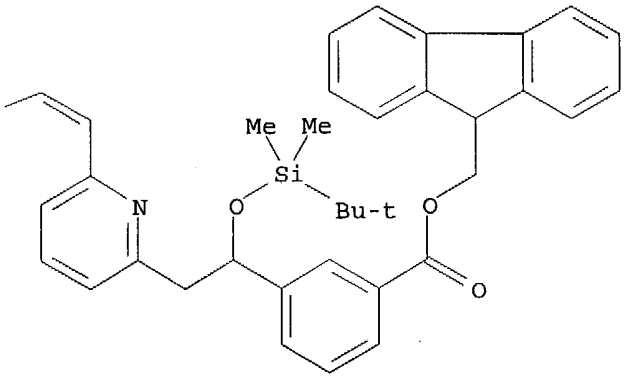
RN 341990-77-0 HCAPLUS
CN Benzoic acid, 3-[2-[6-[3-[1-[[[[4-[[(2R)-2-carboxy-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]ethyl]dithio]phenyl]methoxy]carbonyl]amino]-2,2,2-trifluoroethoxy]-1-undecenyl]-2-pyridinyl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-, 1-(9H-fluoren-9-ylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A

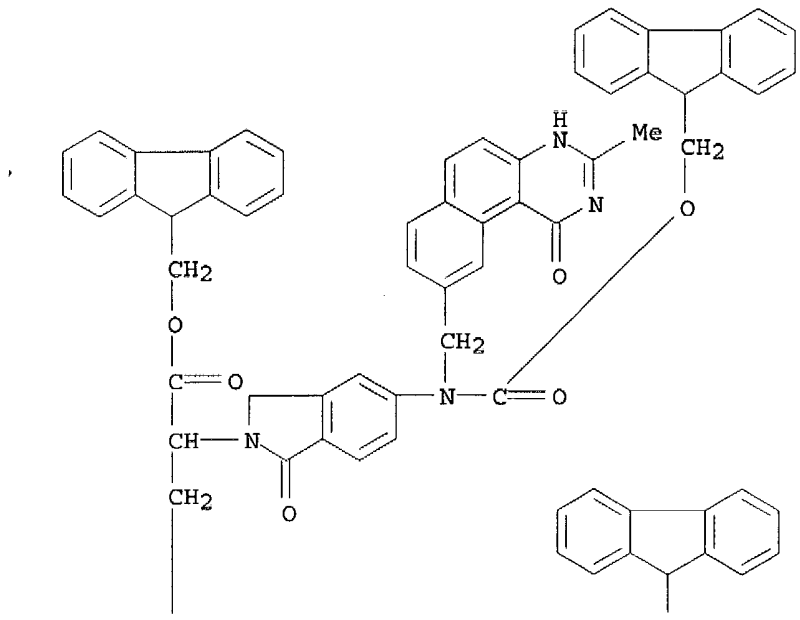


PAGE 1-B

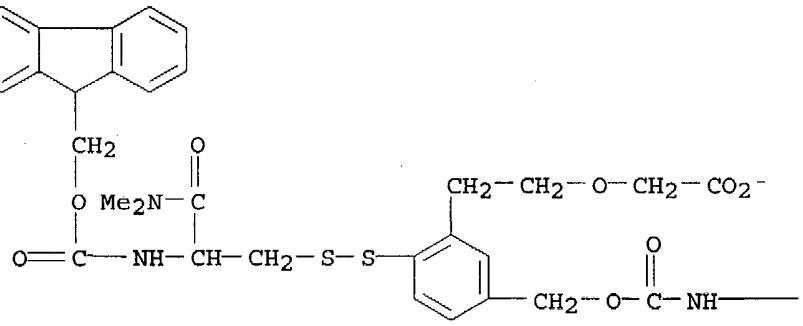


RN 341990-90-7 HCAPLUS
CN Cuprate(1-), [9H-fluoren-9-ylmethyl α-[3-[[4,5-bis[[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-(hydroxy-κO)phenyl]methylene]amino-κN]-8-[[[[3-[2-(carboxymethoxy)ethyl]-4-[[3-(dimethylamino)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-3-oxopropyl]dithio]phenyl]methoxy]carbonyl]amino]octyl]amino]-3-oxopropyl]-5-[[(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl][(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,3-dihydro-1-oxo-2H-isoindole-2-acetato(3-)]-, hydrogen (9CI) (CA INDEX NAME)

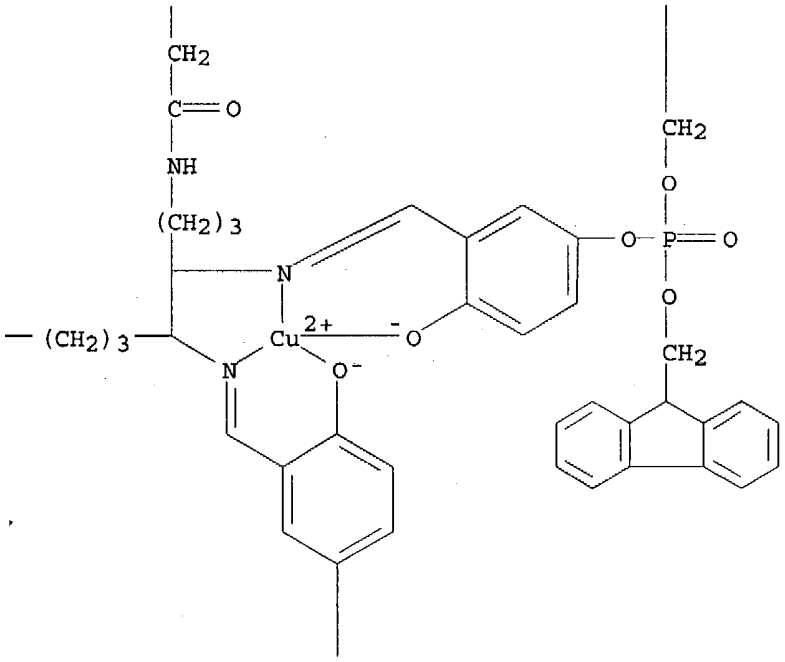
PAGE 1-B



PAGE 2-A



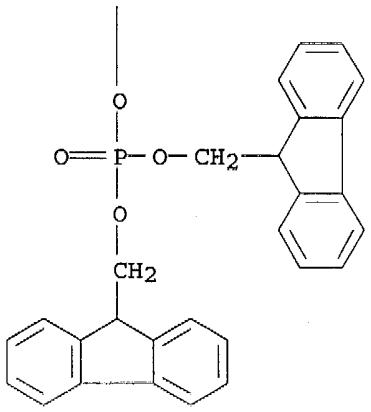
PAGE 2-B



PAGE 3-A

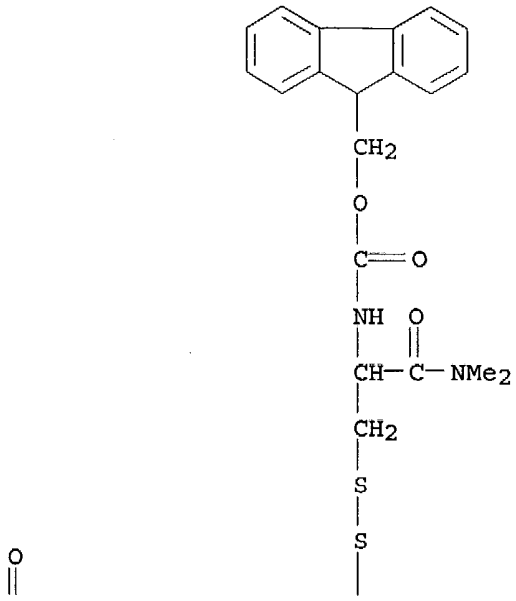
● H^+

PAGE 3-B

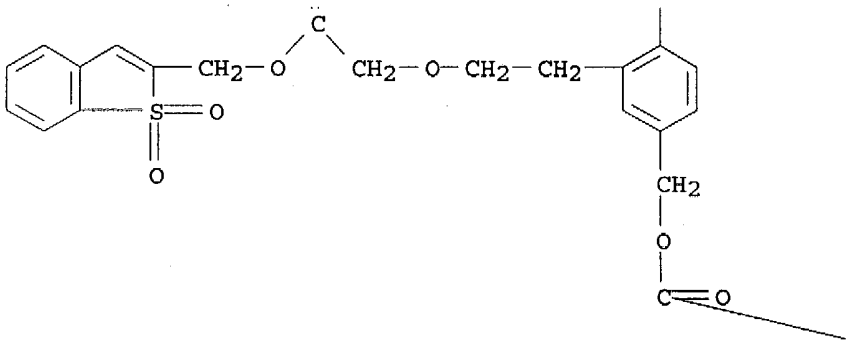


RN 341990-91-8 HCAPLUS
CN Copper, [(1,1-dioxidobenzo[b]thien-2-yl)methyl [2-[5-[[[[[8-amino-4,5-bis[[[5-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]-2-(hydroxy-κO)phenyl]methylene]amino-κN]octyl]amino]carbonyl]oxy]methyl]-2-[[3-(dimethylamino)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-3-oxopropyl]dithio]phenyl]ethoxy]acetato(2-)]- (9CI) (CA INDEX NAME)

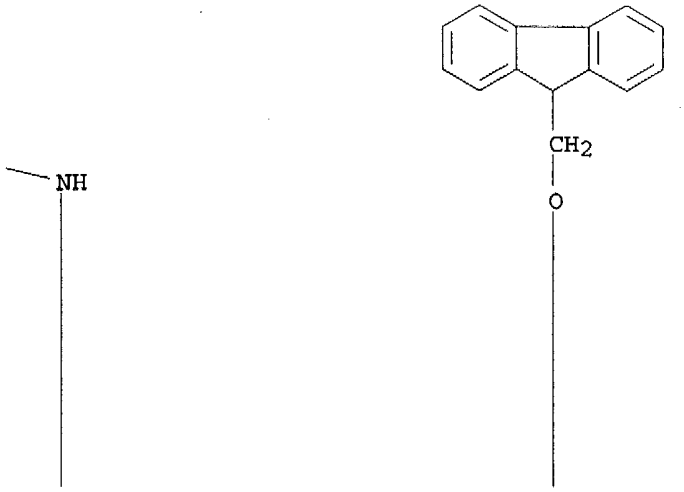
PAGE 1-A



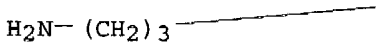
PAGE 2-A

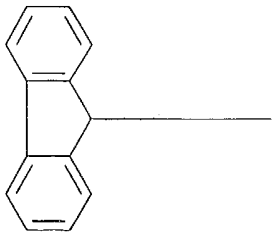


PAGE 2-B

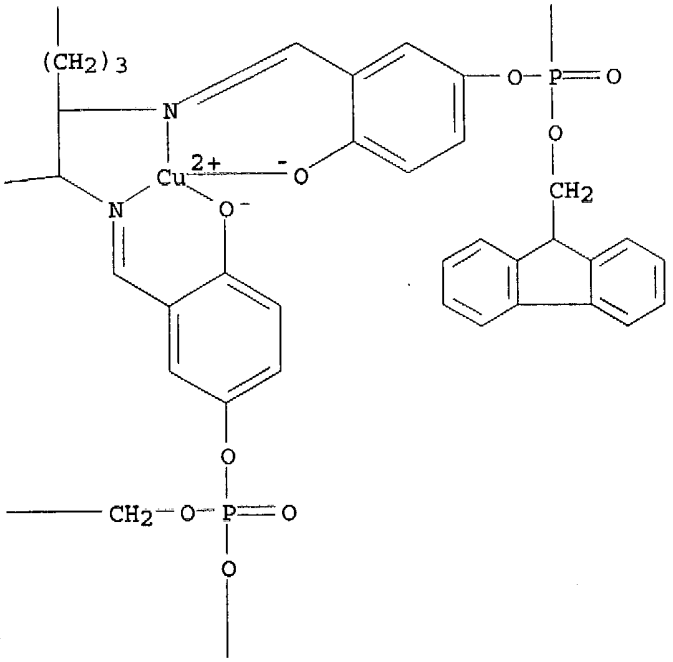


PAGE 3-A

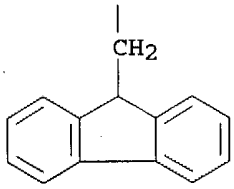




PAGE 3-B

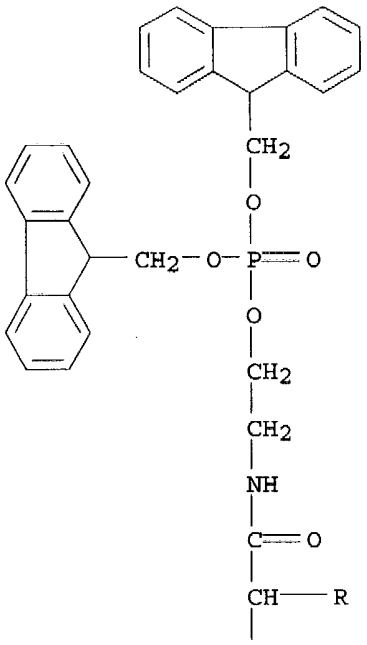


PAGE 4-B

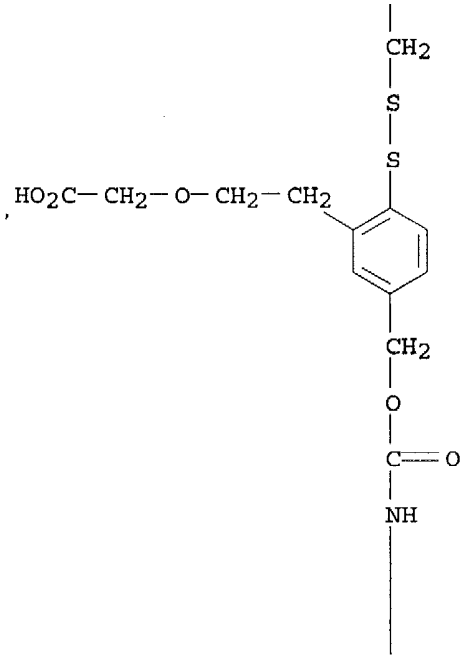


RN 341990-93-0 HCAPLUS
CN Cuprate(1-), [1-[[4-[[3-[[2-[[bis(9H-fluoren-9-ylmethoxy)phosphinyl]oxy]ethyl]amino]-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-3-oxopropyl]dithio]-3-[2-(carboxymethoxy)ethyl]phenyl]methyl] 11,14-bis[(carboxy-κO)methyl]-8-[2-[[4-[5-[[(1,2-dihydro-3-methyl-1-oxobenzo[f]quinazolin-9-yl)methyl][(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-5-(9H-fluoren-9-ylmethoxy)-1,5-dioxopentyl]amino]ethyl]-9-oxo-5-oxa-2,8,11,14-tetraazahexadecanedioato(4-)-κN11,κN14,κO16]-, hydrogen (9CI) (CA INDEX NAME)

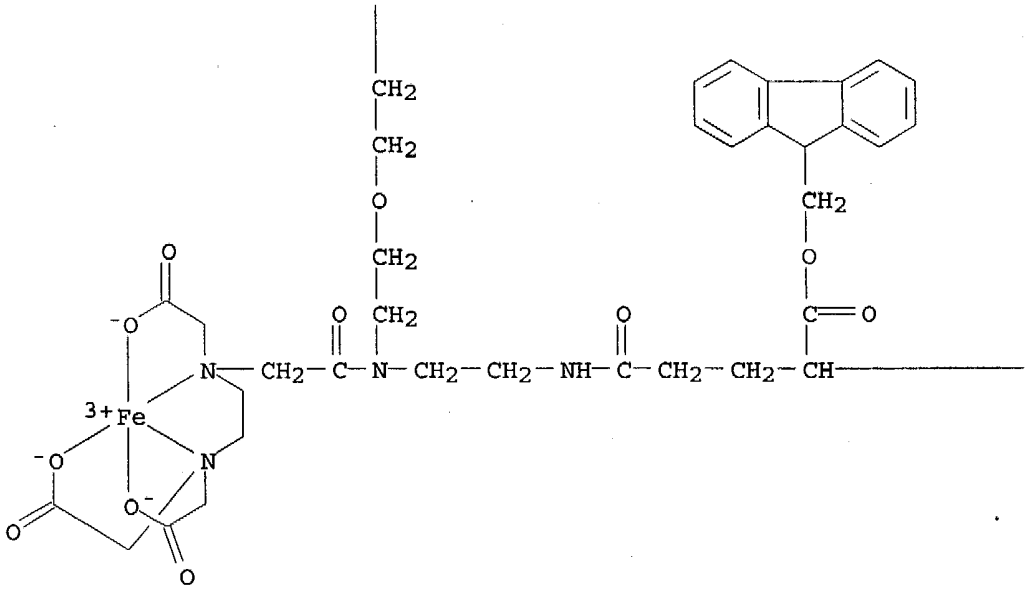
PAGE 1-A



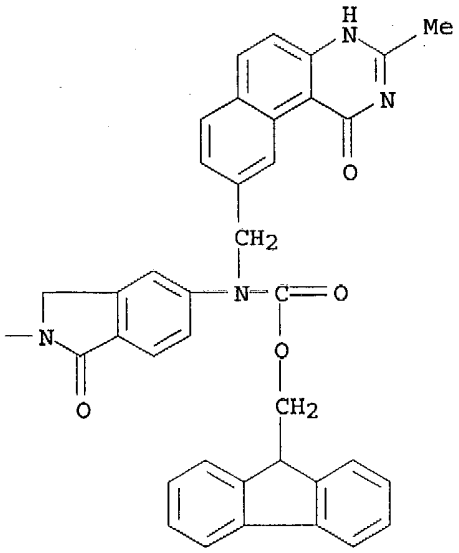
PAGE 2-A

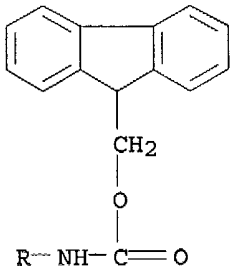


PAGE 3-A



PAGE 3-B



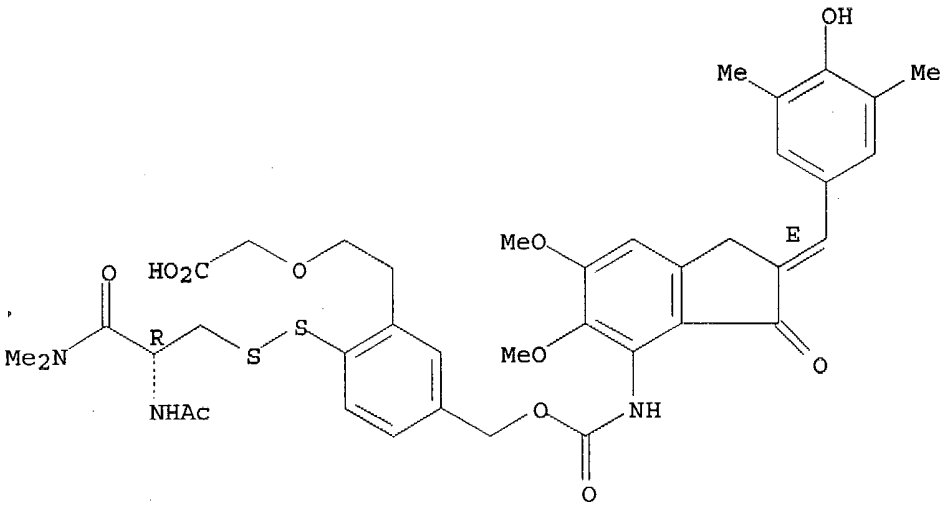


IT **341549-56-2P 341549-59-5P**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

RN 341549-56-2 HCAPLUS

CN Acetic acid, [2-[2-[[(2R)-2-(acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[[[(2E)-2,3-dihydro-2-[(4-hydroxy-3,5-dimethylphenyl)methylene]-5,6-dimethoxy-3-oxo-1H-inden-4-yl]amino]carbonyl]oxy]methyl]phenyl]ethoxy]- (9CI) (CA INDEX NAME)

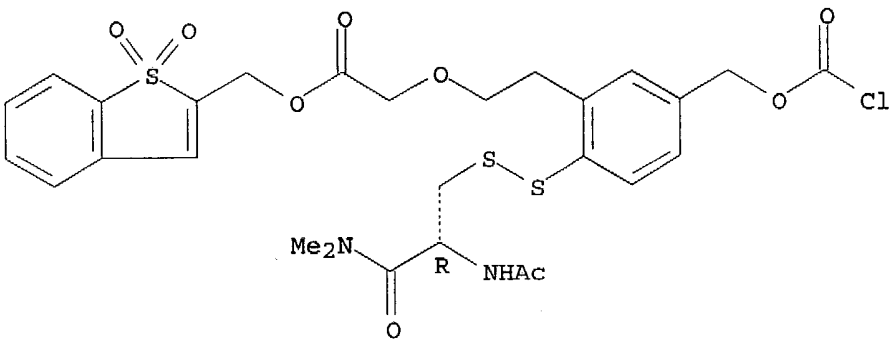
Absolute stereochemistry.
Double bond geometry as shown.



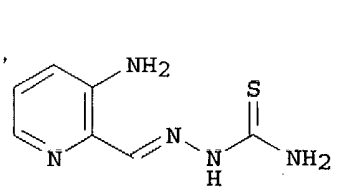
RN 341549-59-5 HCAPLUS

CN Acetic acid, [2-[2-[[(2R)-2-(acetylamino)-3-(dimethylamino)-3-oxopropyl]dithio]-5-[[(chlorocarbonyl)oxy]methyl]phenyl]ethoxy]-, (1,1-dioxidobenzo[b]thien-2-yl)methyl ester (9CI) (CA INDEX NAME)

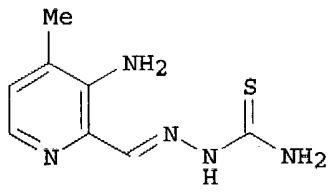
Absolute stereochemistry.



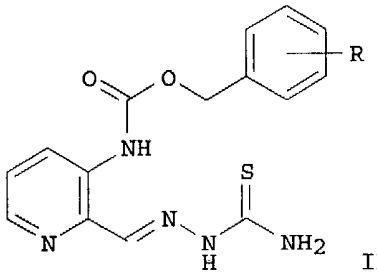
L14 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:100344 HCAPLUS
DOCUMENT NUMBER: 134:295719
TITLE: Syntheses and antitumor activities of potent inhibitors of ribonucleotide reductase: 3-amino-4-methylpyridine-2-carboxaldehyde-thiosemicarbazone (3-Amp), 3-amino-pyridine-2-carboxaldehyde-thiosemicarbazone (3-Ap) and its water-soluble prodrugs
AUTHOR(S): Li, Jun; Zheng, Li-Mou; King, Ivan; Doyle, Terrence W.; Chen, Shu-Hui
CORPORATE SOURCE: Vion Pharmaceuticals, Inc., New Haven, CT, 06511, USA
SOURCE: Current Medicinal Chemistry (2001), 8(2), 121-133
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:295719
GI



I



II



III

AB The reductive conversion of ribonucleotides to deoxyribonucleotides by ribonucleotide reductase (RR) is a crucial and rate-controlling step in the pathway leading to the biosynthesis of DNA, since deoxyribonucleotides

are present in extremely low levels in mammalian cells. Mammalian ribonucleotide reductase (RR) is composed of two dissimilar proteins, often referred to as R1, which contains polythiols and R2, which contains non-heme iron and a free tyrosyl radical. Both the R1 and R2 subunits contribute to the active site of the enzyme. Currently, there are two broad classes of RR inhibitors. The first class includes nucleoside analogs which bind to the R1 subunit of the enzyme, several of which are in development. Among those, Gemcitabine and MDL 101,731 have demonstrated impressive efficacy against various solid tumors. Gemcitabine has now been approved for the treatment of pancreatic cancer and non-small cell lung cancer. The most promising second class of inhibitors of RR includes HCTs [α-(N)-heterocyclic carboxaldehyde thiosemicarbazones, e.g., I and II], which exert enzyme inhibitory effect through high affinity binding with non-heme iron. Based on the clin. success achieved by Gemcitabine, it seems reasonable that a strong inhibitor of RR, which is essential for cellular replication, would be a useful addition to the existing therapeutic agents against cancer. In this chapter, we wish to report several highly efficient syntheses for both I and II based upon palladium mediated Stille/Suzuki/Heck coupling reactions. Based upon the in vivo efficacy profile observed with these two agents, I was chosen over II as the candidate for further optimization with the intention to improve its biol. and pharmaceutical properties. In this vein, we have synthesized two water soluble phosphate containing prodrugs III [R = 2-(HO)2P(O)O, 4-(HO)2P(O)O] and one disulfide-linked prodrug of 3-AP III (R = 2-H2NCH2CH2SS). As expected, bioconversion study using either alkaline phosphatase or glutathione showed that these prodrugs were indeed converted to the parent I. When evaluated against the murine M-109 lung carcinoma as well as the B16-F10 murine melanoma xenograft models, the newly prepared phosphate prodrugs displayed improved efficacy and safety profiles than that found with the parent. More significantly, the ortho-phosphate prodrug III [R = 2-(HO)2P(O)O] demonstrated impressive antitumor effect using once-a-day dosing regimen. In summary, the results disclosed herein demonstrated that some of I prodrugs prepared indeed demonstrated improved pharmaceutical, biol. and toxicity profiles over the parent I. Efforts directed towards further optimization of I prodrugs as novel anticancer agents is clearly warranted.

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT **334765-95-6P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and antitumor activities of heterocyclic carboxaldehyde semicarbazones and their watersol. prodrugs as potent inhibitors of ribonucleotide reductase)

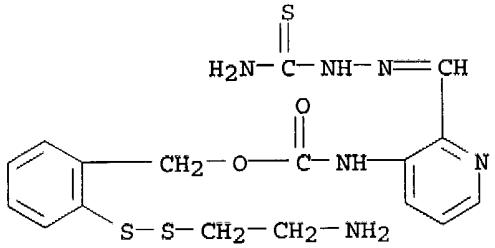
IT 10261-94-6P 14578-18-8P 18699-87-1P 21203-74-7P 25230-59-5P
36625-67-9P 65156-92-5P 116026-99-4P 200933-31-9P 200933-40-0P
208983-72-6P 208983-76-0P 208983-77-1P 208983-78-2P 208983-82-8P
208983-83-9P 208983-84-0P 208983-86-2P 209798-50-5P 216240-63-0P
220257-04-5P 220257-22-7P 334765-84-3P 334765-85-4P 334765-87-6P
334765-88-7P **334765-89-8P 334765-90-1P**
334765-91-2P 334765-92-3P 334765-93-4P
334765-94-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activities of heterocyclic carboxaldehyde semicarbazones and their watersol. prodrugs as potent inhibitors of ribonucleotide reductase)

IT **334765-95-6P**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and antitumor activities of heterocyclic carboxaldehyde semicarbazones and their watersol. prodrugs as potent inhibitors of ribonucleotide reductase)

RN 334765-95-6 HCAPLUS

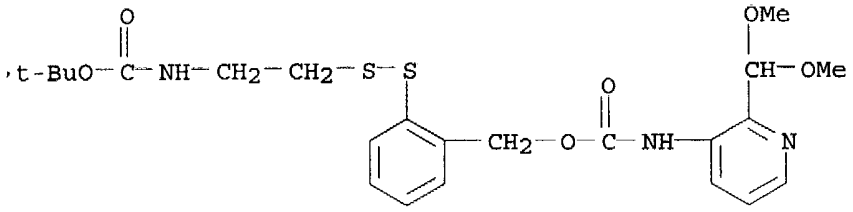
CN Carbamic acid, [2-[[(aminothioxomethyl)hydrazono]methyl]-3-pyridinyl]-, [2-[(2-aminoethyl)dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



IT **334765-89-8P 334765-90-1P 334765-91-2P**
334765-92-3P 334765-93-4P 334765-94-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activities of heterocyclic carboxaldehyde semicarbazones and their watersol. prodrugs as potent inhibitors of ribonucleotide reductase)

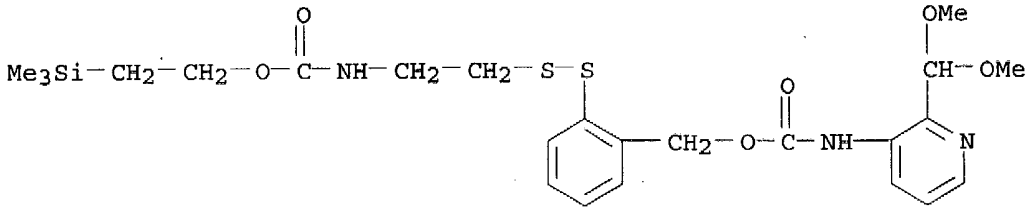
RN 334765-89-8 HCAPLUS

CN Carbamic acid, [2-(dimethoxymethyl)-3-pyridinyl]-, [2-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)

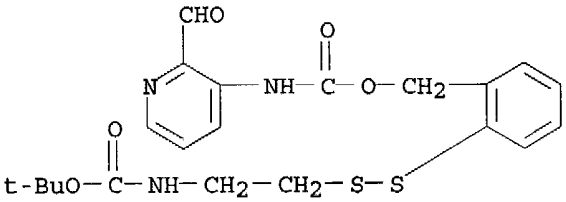


RN 334765-90-1 HCAPLUS

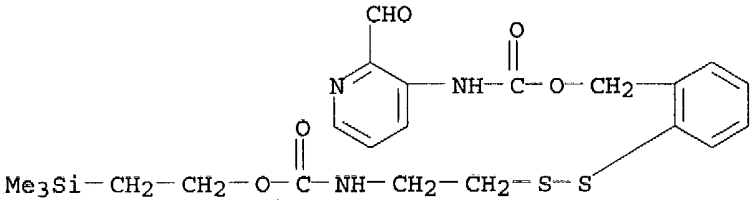
CN Carbamic acid, [2-(dimethoxymethyl)-3-pyridinyl]-, [2-[[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



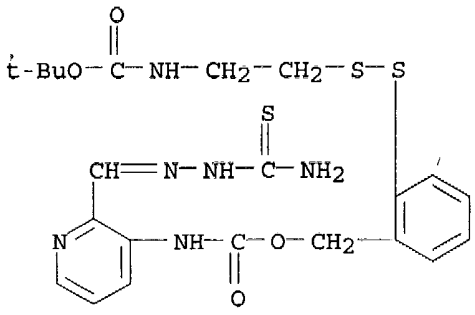
RN 334765-91-2 HCAPLUS
CN Carbamic acid, (2-formyl-3-pyridinyl)-, [2-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



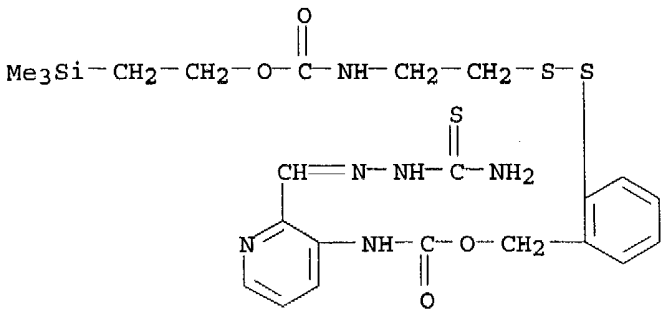
RN 334765-92-3 HCAPLUS
CN Carbamic acid, (2-formyl-3-pyridinyl)-, [2-[[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



RN 334765-93-4 HCAPLUS
CN Carbamic acid, [2-[[(aminothioxomethyl)hydrazono]methyl]-3-pyridinyl]-, [2-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



RN 334765-94-5 HCAPLUS
CN Carbamic acid, [2-[[(aminothioxomethyl)hydrazono]methyl]-3-pyridinyl]-, [2-[[2-[[[2-(trimethylsilyl)ethoxy]carbonyl]amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:772487 HCAPLUS
DOCUMENT NUMBER: 133:340248
TITLE: Conjugate having a cleavable linkage for use in a **liposome**
INVENTOR(S): Zalipsky, Samuel; Gabizon, Alberto A.
PATENT ASSIGNEE(S): Alza Corporation, USA; Hadasit Medical Research Services & Development Ltd.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064484	A2	20001102	WO 2000-US10922	20000421
WO 2000064484	A3	20011115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173222	A2	20020123	EP 2000-928321	20000421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6365179	B1	20020402	US 2000-556610	20000421
JP 2002542302	T2	20021210	JP 2000-613474	20000421
AU 769425	B2	20040129	AU 2000-46577	20000421
NO 2001005144	A	20011211	NO 2001-5144	20011022
ZA 2001008724	A	20021023	ZA 2001-8724	20011023
ZA 2001008726	A	20030305	ZA 2001-8726	20011023
US 2003054028	A1	20030320	US 2002-57839	20020125
US 2003211079	A1	20031113	US 2003-371169	20030221

PRIORITY APPLN. INFO.:
US 1999-130897P P 19990423
US 2000-556056 A1 20000421
US 2000-556610 A1 20000421
WO 2000-US10922 W 20000421

US 2001-982336 A1 20011015

OTHER SOURCE(S): MARPAT 133:340248

AB Conjugates of a hydrophobic moiety, such as a lipid, linked through a cleavable dithiobenzyl linkage to a therapeutic agent are described. The dithiobenzyl linkage is susceptible to cleavage by mild thiolysis, resulting in release of the therapeutic agent in its original form. The linkage is stable under nonreducing conditions. The conjugate can be incorporated into **liposomes** for administration in vivo and release of the therapeutic agent in response to endogeneous in vivo reducing conditions or in response to administration of an exogenous reducing agent. P-diacyldiglyceroldithiobenzal-mitomycin C was prepared, and combined with hydrogenated soy phosphatidylcholine (HSPC) and distearoyl phosphatidylethanolamine derivatized with methoxy polyethylene glycol (mPEG-DSPE) in a molar ratio of 5/90/5, and dissolved in ethanol to obtain a **liposome** formulation and for its pharmacokinetic study in vivo.

IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST **liposome** conjugate dithiobenzyl lipid prepn; mitomycin dithiobenzyl glyceride conjugate prepn **liposome**

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

IT Drug delivery systems
(**liposomes**; conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

IT 50-07-7DP, Mitomycin C, conjugates with lipids through dithiobenzyl linkages **303983-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

IT 50-91-9D, conjugates with lipids through dithiobenzyl linkages 51-21-8D, 5-Fluorouracil, conjugates with lipids through dithiobenzyl linkages 51-55-8D, Atropine, conjugates with lipids through dithiobenzyl linkages 54-42-2D, Iododeoxyuridine, conjugates with lipids through dithiobenzyl linkages 56-54-2D, Quinidine, conjugates with lipids through dithiobenzyl linkages 59-05-2D, Methotrexate, conjugates with lipids through dithiobenzyl linkages 147-94-4D, conjugates with lipids through dithiobenzyl linkages 305-03-3D, Chlorambucil, conjugates with lipids through dithiobenzyl linkages 4055-39-4D, Mitomycin A, conjugates with lipids through dithiobenzyl linkages 5536-17-4D, Vidarabine, conjugates with lipids through dithiobenzyl linkages 11056-06-7D, Bleomycin, conjugates with lipids through dithiobenzyl linkages 20830-81-3D, Daunorubicin, conjugates with lipids through dithiobenzyl linkages 23214-92-8D, Doxorubicin, conjugates with lipids through dithiobenzyl linkages 30516-87-1D, AZT, conjugates with lipids through dithiobenzyl linkages 33419-42-0D, Etoposide, conjugates with lipids through dithiobenzyl linkages 53910-25-1D, Pentostatin, conjugates with lipids through dithiobenzyl linkages 59277-89-3D, Acyclovir, conjugates with lipids through dithiobenzyl linkages 65271-80-9D, Mitoxantrone, conjugates with lipids through dithiobenzyl linkages
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

IT 50-07-7, Mitomycin C 57-11-4, Stearic acid, reactions 96-27-5,

3-Mercapto-1,2-propanediol 53339-53-0, 4-Mercaptobenzyl alcohol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

IT 4807-52-7P 89067-85-6P 303983-01-9P 303983-02-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

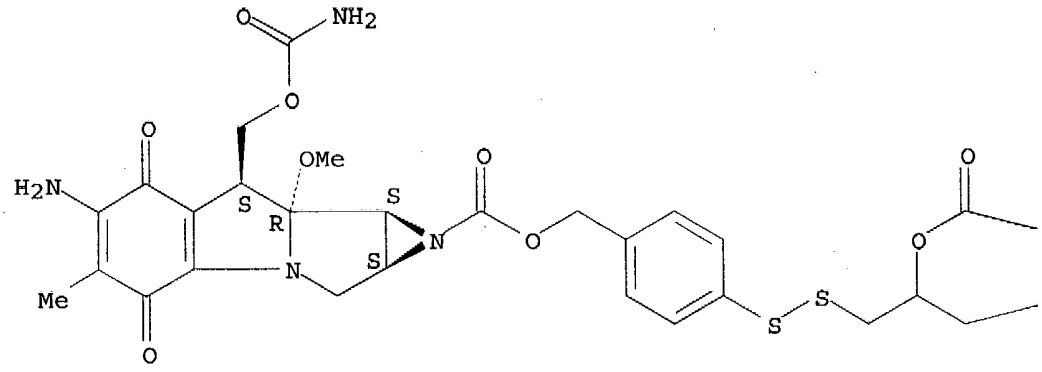
IT **303983-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of hydrophobic moiety having cleavable dithiobenzyl linkages for use in **liposomes**)

RN 303983-00-8 HCAPLUS

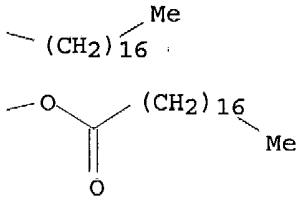
CN Azirino[2',3':3,4]pyrrolo[1,2-a]indole-1(2H)-carboxylic acid, 6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxo-, [4-[[2,3-bis[(1-oxooctadecyl)oxy]propyl]dithio]phenyl]methyl ester, (1aS,8S,8aR,8bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:772486 HCAPLUS
DOCUMENT NUMBER: 133:340247
TITLE: Releasable linkage and compositions containing same
INVENTOR(S): Zalipsky, Samuel
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064483	A2	20001102	WO 2000-US10830	20000421
WO 2000064483	A3	20010802		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173221	A2	20020123	EP 2000-923572	20000421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6365179	B1	20020402	US 2000-556610	20000421
JP 2002542386	T2	20021210	JP 2000-613473	20000421
NZ 514990	A	20040130	NZ 2000-514990	20000421
AU 770390	B2	20040219	AU 2000-43672	20000421
NO 2001005169	A	20011219	NO 2001-5169	20011023
ZA 2001008724	A	20021023	ZA 2001-8724	20011023
ZA 2001008726	A	20030305	ZA 2001-8726	20011023
US 2003054028	A1	20030320	US 2002-57839	20020125
US 2003211079	A1	20031113	US 2003-371169	20030221

PRIORITY APPLN. INFO.:
US 1999-130897P P 19990423
US 2000-556056 A1 20000421
US 2000-556610 A1 20000421
WO 2000-US10830 W 20000421
US 2001-982336 A1 20011015

AB A compound comprised of a hydrophilic polymer covalently yet reversibly linked to an amine-containing ligand through a dithiobenzyl linkage is described. O- and p-methoxy polyethylene glycol-urethane-ethyldithiobenzyl-distearoylphosphatidyl ethanolamine were prepared and combined with dioleoyl phosphatidylehtanolamine (DOPE) to obtain **liposomes** having an average diameter of 100 nm.

IC ICM A61K047-48
CC 63-6 (Pharmaceuticals)
ST conjugate polyethyleneglycol dithiobenzyl amine contg drug; **liposome** conjugate amine hydrophilic polymer dithiobenzyl
IT Drug delivery systems
(**liposomes**, injections; conjugates of amine-containing drugs with hydrophilic polymers through dithiobenzyl linkages)
IT Drug delivery systems
(**liposomes**; conjugates of amine-containing drugs with hydrophilic

polymers through dithiobenzyl linkages)

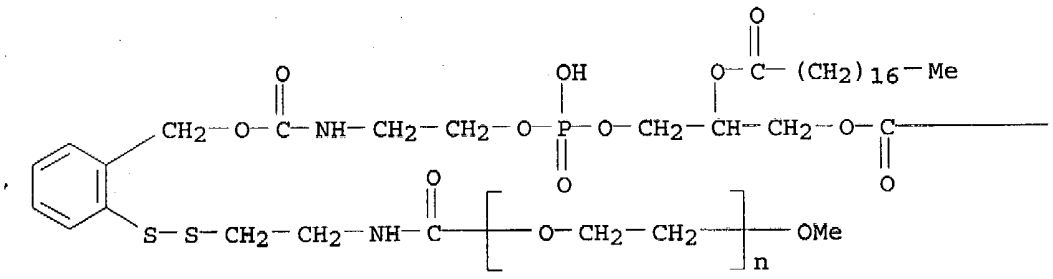
IT **304013-00-1P 304013-02-3P 304013-04-5P**
304013-06-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of amine-containing drugs with hydrophilic polymers through dithiobenzyl linkages)

IT 926-25-0P 1437-71-4P 1437-90-7P, 5-Methylthiazolidine-2-thione
1437-92-9P 4146-02-5P 4146-16-1P 124661-64-9P 304013-12-5P
304013-14-7P 304013-16-9P 304013-18-1P 304013-19-2P
304013-20-5P 304013-21-6P **304013-22-7P**
304013-29-4P 304013-31-8P 304013-33-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of conjugates of amine-containing drugs with hydrophilic polymers through dithiobenzyl linkages)

IT **304013-00-1P 304013-02-3P 304013-04-5P**
304013-06-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of amine-containing drugs with hydrophilic polymers through dithiobenzyl linkages)

RN 304013-00-1 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[2-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-yl]phenyl]dithio]ethyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A

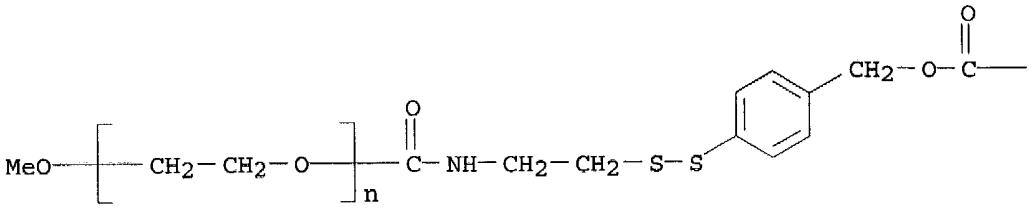


PAGE 1-B

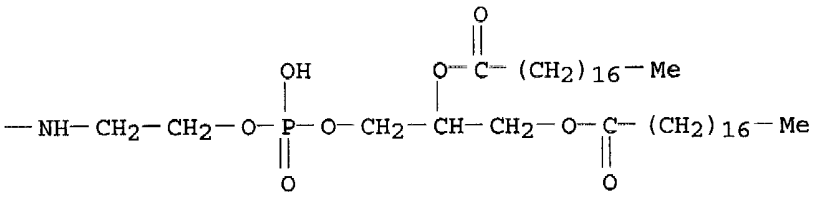
— $(CH_2)_{16}$ — Me

RN 304013-02-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-yl]phenyl]dithio]ethyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A

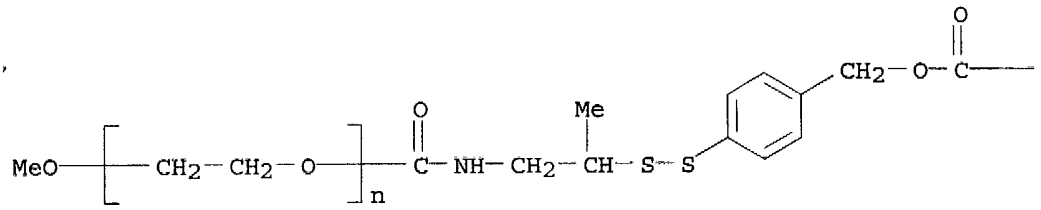


PAGE 1-B

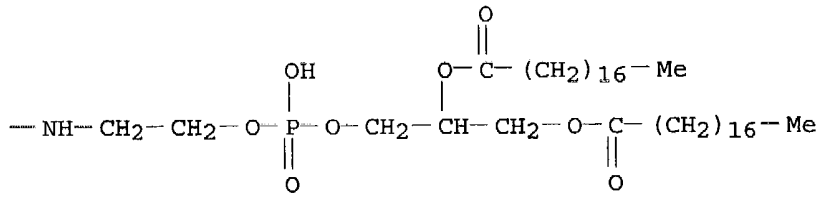


RN 304013-04-5 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-yl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



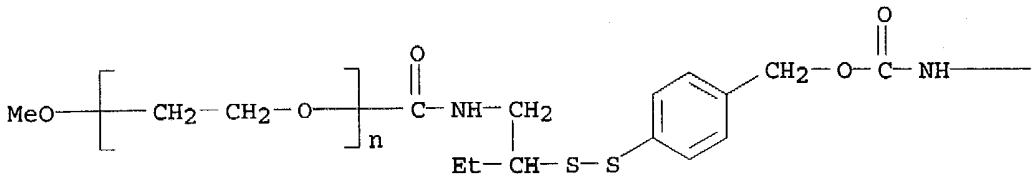
PAGE 1-B



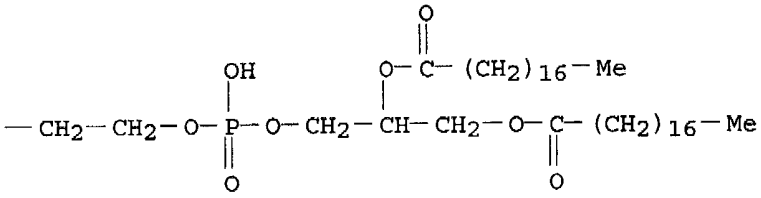
RN 304013-06-7 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[8-hydroxy-8-oxido-3,14-dioxo-11-[(1-oxooctadecyl)oxy]-2,7,9,13-tetraoxa-4-aza-8-phosphahentriacont-1-

yl]phenyl]dithio]butyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

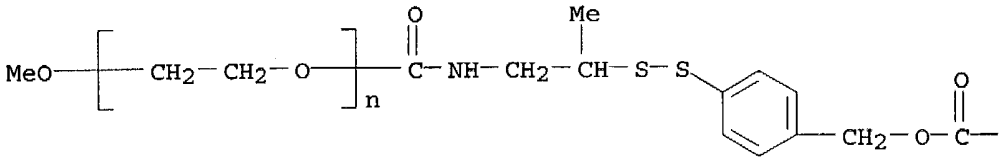


IT **304013-20-5P 304013-22-7P 304013-29-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of conjugates of amine-containing drugs with hydrophilic polymers
through dithiobenzyl linkages)

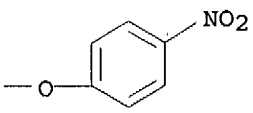
RN 304013-20-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]propyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



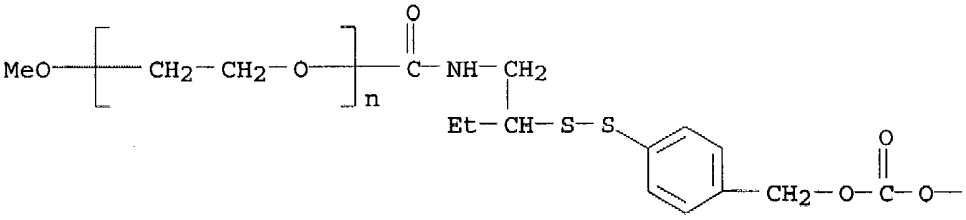
PAGE 1-B



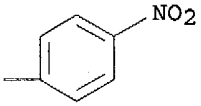
RN 304013-22-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]butyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A

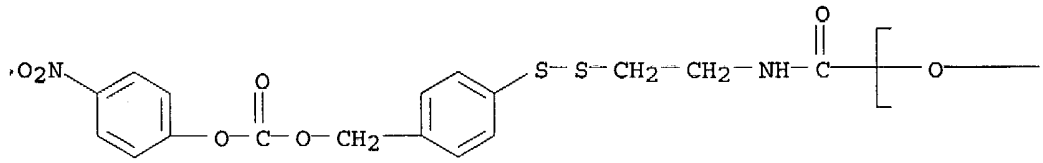


PAGE 1-B

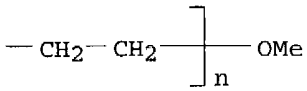


RN 304013-29-4 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[2-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]dithio]ethyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



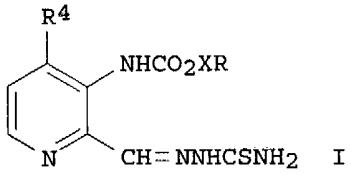
L14 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:414736 HCAPLUS
DOCUMENT NUMBER: 129:67710
TITLE: Prodrug forms of ribonucleotide reductase inhibitors 3-AP and 3-AMP
INVENTOR(S): Li, Jun; Niu, Chuan-Sheng; Li, Xiuyan; Doyle, Terrence

W.; Chen, Shu-Hui
PATENT ASSIGNEE(S): Vion Pharmaceuticals, Inc., USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5767134	A	19980616	US 1997-856568	19970515
WO 9851669	A1	19981119	WO 1998-US9750	19980514
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874840	A1	19981208	AU 1998-74840	19980514
AU 727848	B2	20010104		
EP 988285	A1	20000329	EP 1998-922247	19980514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9809633	A	20000711	BR 1998-9633	19980514
JP 2001526664	T2	20011218	JP 1998-549484	19980514
RU 2199531	C2	20030227	RU 1999-127343	19980514
MX 9910422	A	20000831	MX 1999-10422	19991112

PRIORITY APPLN. INFO.: US 1997-856568 A 19970515
WO 1998-US9750 W 19980514

OTHER SOURCE(S): MARPAT 129:67710
GI

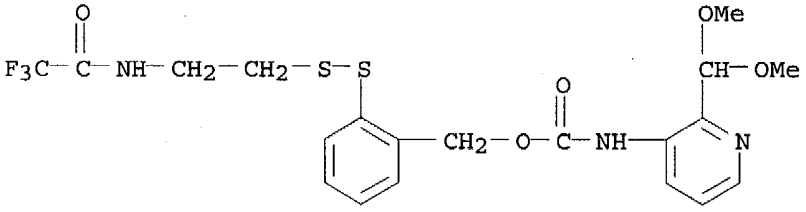


I

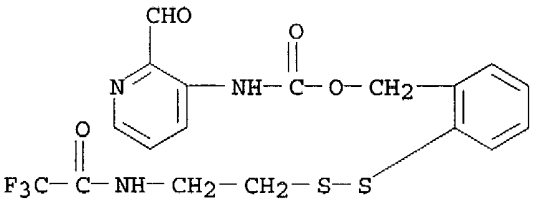
AB The present invention relates to novel prodrug forms I [X = CHR1, CHR1C6H4-p, CHR1C6H4-o; R = OP(O)(ONa)2, S2R2; R1 = H, alkyl; R2 = CH2CH2R3, CH2CO2H; R3 = NH2, NHAc, OH; R4 = H, Me] of ribonucleoside diphosphate reductase inhibitors 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (3-AP) 3-amino-4-methylpyridine-2-carboxaldehyde thiosemicarbazone (3-AMP) which have increased water solubility, bioavailability and resistance to in vivo acetylation of their amino functions. Thus, I [X = CH2C6H4-p, R = OP(O)(ONa)2, R4 = H, II] was prepared from 2-chloronicotinic acid and 4-HOCH2C6H4OP(O)(OCH2CH2SiMe3)2 in 7 steps. II had 300 times the soly in water of 3-AP and also showed better bioavailability.

IC ICM A61K031-44

ICS C07D213-02
NCL 514353000
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
IT 25230-59-5P, Methyl 2-formylnicotinate 40134-18-7P, Methyl 2-chloronicotinate 208983-73-7P 208983-74-8P 208983-75-9P 208983-76-0P 208983-77-1P 208983-80-6P 208983-81-7P 208983-82-8P 208983-83-9P 208983-86-2P 208983-87-3P 208983-89-5P 208983-90-8P 208983-92-0P **208983-93-1P 208983-94-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prodrug forms of aminopyridinecarboxaldehyde thiosemicarbazone ribonucleotide reductase inhibitors)
IT 208983-84-0P 208983-85-1P 208983-91-9P **208983-95-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrug forms of aminopyridinecarboxaldehyde thiosemicarbazone ribonucleotide reductase inhibitors)
IT **208983-93-1P 208983-94-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prodrug forms of aminopyridinecarboxaldehyde thiosemicarbazone ribonucleotide reductase inhibitors)
RN 208983-93-1 HCAPLUS
CN Carbamic acid, [2-(dimethoxymethyl)-3-pyridinyl]-, [2-[[2-[(trifluoroacetyl)amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)

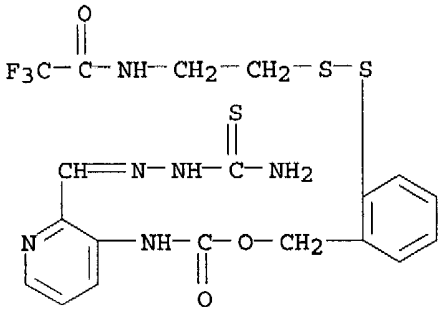


RN 208983-94-2 HCAPLUS
CN Carbamic acid, (2-formyl-3-pyridinyl)-, [2-[[2-[(trifluoroacetyl)amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



IT **208983-95-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrug forms of aminopyridinecarboxaldehyde thiosemicarbazone ribonucleotide reductase inhibitors)

RN 208983-95-3 HCAPLUS
CN Carbamic acid, [2-[[(aminothioxomethyl)hydrazono]methyl]-3-pyridinyl]-, [2-[[2-[(trifluoroacetyl)amino]ethyl]dithio]phenyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT